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EFFECT OF PENICILLIN IN THE TREATMENT OF INFANTILE CONGENITAL SYPHILIS

Further Observations

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IN THE year that has elapsed since our preliminary note,[1] 122 additional cases of manifest congenital syphilis in children under 2 years of age have been treated by the university groups at New Orleans, Philadelphia, Baltimore and Galveston. This brings the total number now suitable for analysis to 191. Among these are 84 Negro boys, 84 Negro girls, 10 white boys and 13 white girls. The mean age at start of treatment was 164 days, with range from 11 days to 23 months. Pretreatment studies have been adequate for all, and no therapy other than intramuscular injection of penicillin has been employed. Total dosages have ranged from 770 to 150,000 units per kilogram of body weight; the smaller of these represents the amount received by a moribund infant of 5 weeks who died during the first day of treatment. The smallest total dosage received by any infant who completed treatment was 12,000 units per kilogram of body weight;

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1. Platou, R. V.; Hill, A. J.; Ingraham, N. R.; Goodwin, M. S.; Wilkinson, E. E., and Hansen, A. E.: Penicillin in the Treatment of Infantile Congenital Syphilis: A Brief Preliminary Note, J. A. M. A. **127**:582 (March 10) 1945.

the majority have been treated with schedules of 20,000, 40,000 or 80,000 units per kilogram of body weight. Penicillin has been administered in aqueous or saline solution (preferably the former), usually every three hours for approximately sixty doses over a period of seven and one-half days. Recently, some infants receiving dosage schedules of 80,000 or more units per kilogram of body weight have had the drug divided into one hundred and twenty equal injections given over a period of fifteen days.

When rapid shifts in population so prevalent in these times are considered, follow-up observations have been obtained for a gratifyingly large number. Though delinquencies have increased as the study progressed, combined data are adequate for a number of conclusions. From these, certain recommendations concerning the use of penicillin in early infantile congenital syphilis may be made, though the ideal method has not yet been defined. In the socioeconomic class from which most of these cases are drawn, the prevalence of serious complicating factors is obviously great, and the prognosis for any one must be considered proportionately grave.

Of greatest importance, now as always, is diligent adjunctive and supportive care, according to well recognized pediatric principles. In some of these syphilitic infants penicillin therapy has been withheld for several days or weeks after diagnosis while intercurrent infections, nutritional deficiencies and metabolic disturbances were corrected or improved. Whether such a short period of delay is important in relation to rate of survival or cure of syphilis cannot be stated at present. In recent months, since penicillin has become more readily available, patients have been treated more promptly after diagnosis, other appropriate corrective measures being employed simultaneously. We believe that the latter plan constitutes no additional hazard for the syphilitic infant and may possibly also reduce the risk of death from syphilis per se.

The results which are to be presented in this paper must be interpreted in the light of the fact that from June 1943, the date of inception of the study, to the present, commercial penicillin has been a changing mixture of various substances. The content of "impurities" has gradually decreased as potency, in terms of units per milligram, has increased. The relative amounts of the several identified penicillin fractions G, F, X and K have likewise varied from time to time. These two changes, and perhaps others, suggest that therapeutic efficacy may not have remained constant and that it may be significantly different today than it was originally. It is not now possible to assess the extent to which these changes may have affected the results here reported.

REACTIONS TO TREATMENT

Other than the febrile reactions noted in the accompanying table (table 1), there were only eight others which might be legitimately designated as therapeutic shocks. These were all transient, and none were severe enough to interrupt or modify the plan of treatment already initiated. Any of these reactions might have occurred without relation to therapy, and their classification as therapeutic shock is therefore admittedly arbitrary.

1. A preexisting convulsive disorder appeared to be aggravated by the disturbance of multiple intramuscular injections.

2. Edema and hematuria developed in 1 infant early in the course of penicillin therapy but cleared uneventfully. A diagnosis of syphilitic nephritis could not be objectively established.

3. Persistent hyperemesis during the first three days of treatment subsided uneventfully.

TABLE 1.—*Reactions to Treatment in Early Manifest Congenital Syphilis*

Reaction	Number	Percentage
None	103	51
Not recorded	15	7
Febrile I	22	11
Febrile II	45	22
Febrile III	18	9
Others *	8	..
Total reactions	211	
Total courses	204	
Total patients	191	

* These reactions were also accompanied by fever.

4. A definite cutaneous Herxheimer reaction occurred, along with sudden, nearly fatal collapse forty-eight hours after treatment was begun. This responded to symptomatic measures, and treatment was resumed.

5 and 6. Transient urticarial eruption appeared but responded immediately to symptomatic measures. These were probably due to impurities in particular lots of penicillin.

7 and 8. Cutaneous lesions were accentuated, and dactylitis appeared forty-eight hours after the first injection of penicillin; these were considered as probable evidences of therapeutic shock.

Because most of the treated infants had associated nonsyphilitic infections, it was necessary to define arbitrarily the febrile reactions observed. Many of those so listed might have been due to causes other than therapeutic shock. "Febrile, grade I" is defined as a rise in temperature of not more than 1 degree Fahrenheit from the pretreatment

level; "grade II" is a rise of from 1 to 2 degrees above pretreatment level, and "grade III" any rise over 2 degrees.

From our experience there seems no justification for gradually building up the dosage of penicillin for avoidance of Herxheimer reactions. In this series the total amount of the drug to be employed in any case has been divided equally into the required number of injections with no such early precaution. This is in conformity with the experience of those treating early acquired syphilis in adults.[2]

We have noted incidentally that injections of sodium penicillin in distilled water appear to be consistently less painful than those in isotonic solution of sodium chloride.

RESULTS

Early effects on the observed clinical lesions were little short of dramatic. In no case were positive results secured on dark field examination beyond twenty-four hours after treatment was initiated; cutaneous and mucosal syphilids almost invariably were visibly resolving within one to three days and cleared before the course of therapy had been completed. Probably because of extensive secondary infections, rhinitis, though greatly improved, usually persisted in some degree for three to six weeks. Among those patients exhibiting obvious malnutrition, rapid gain in weight was frequently observed, both during hospitalization and at subsequent visits to the clinic. This "tonic effect" with penicillin therapy was not so striking as has been reported for some cases of neurosyphilis in adults. Osseous lesions have of course responded more slowly, but definite evidences of improvement could be noted during the first few weeks, and healing was usually seen in the roentgenograms after from three to five months. Though comparative studies are not complete, it appears that healing is more rapid following penicillin than with conventional arsenical and heavy metal therapy. Resolution of generalized glandular enlargement and hepatosplenomegaly followed a completely irregular and unpredictable pattern, perhaps related to their duration before treatment was initiated. Improvement in degrees of anemia could not be related to penicillin therapy because transfusions and various hematinics were given to most patients. Anemia was generally attributable to combined physiologic, infectional and nutritional causes; it did not appear in any way to be characteristic of syphilis per se.

Serologic results were interesting (tables 2 and 3). There was a progressive increase in the percentage of cases in which reactions became seronegative from 7.9 per cent among 177 observed for less than two months up to 92.3 per cent of the small number so far followed beyond eighteen months. During these same periods there was a decrease in

2. Moore, J. E.: Personal communication to the authors.

the number continuing to exhibit either progressive decline or unchanging serologic titers. Among 162 infants considered to be clinically well and free of evidences of active syphilis following treatment, serologic relapse alone was observed only six times.

TABLE 2.—*Results Related to Duration of Observation in One Hundred and Ninety-One Cases of Early Manifest Congenital Syphilis*

Time Followed After Start of Treatment, Days	Cases Observed for Specified Time Only	Total No. of Cases Observed for Stated Period	Status at Specified Time: Serologic Status of 162 Patients Clinically Well: Sero-negative No.	%	Declining No.	%	Unchanged No.	%	Serologic Relapse No.	%	Uncertain No.	%	Clinical and Serologic Relapse, No.	Dead,* No.
To 60	41	177	14	7.9	98	55.4	36	20.3	1	0.6	10	5.6	0	18
61-120	29	120	28	23.3	71	59.2	12	10.0	1	0.8	0	...	4	4
121-180	22	96	45	46.9	42	43.8	4	4.2	2	2.1	1	1.04	1	1
181-270	33	82	48	58.5	26	31.7	2	2.4	2	2.4	3	3.7	0	1
271-365	29	56	44	78.6	7	12.5	3	5.4	1	1.8	1	1.8	0	0
366-480	24	34	26	76.4	6	17.6	0	...	0	...	2	5.9	0	0
481	13	13	12	92.3	0	....	0	...	0	...	1	7.7	0	0
Total	191	.....											5 (2.6%)	24 (12.6%)

* Status as to syphilis at the time of death is indicated in table 4.

For purposes of this study, we have designated as serorelapse any case in which the following criteria are satisfied: (1) If at least two preceding serologic tests were negative over a period of at least one month and then became positive in undiluted serum or in any dilution

TABLE 3.—*Results of Observations for Sixty to Four Hundred and Eighty Days After Treatment on One Hundred and Forty-One Infants Treated Only with Sodium Penicillin on Various Dosage Schedules*

Total Dose,* Units/Kg.	Cases, No.	Results † Satisfactory	Unsatisfactory	Uncertain
10,000-19,999	19	16	3	
20,000-29,999	34	24	6	4
30,000-39,999	13	9	4	
• Total <40,000 u./Kg.	66	49 (74.2%)	13 (19.7%)	4 (6.1%)
40,000-79,999	65	59	3	3
80,000	10	8	1	1
Total > 40,000 u./Kg.	75	67 (89.3%)	4 (5.3%)	4 (5.3%)
Total, all schedules	141	116 (82.3%)	17 (12.1%)	8 (5.7%)

* Divided into sixty to one hundred and twenty equal intramuscular injections, given at three hour intervals "around the clock."

† Results were considered satisfactory if the patient was clinically well, with negative or declining serologic titer; unsatisfactory, if the titer was stationary or rising or if there was a clinical or serologic relapse, and uncertain, if observation was insufficient.

of serum, confirmed by two subsequent tests of equal or increasing positivity; or (2) if the preceding serologic tests were positive in a constant or decreasing titer and then two consecutive tests were positive with the titer increasing to a value at least four times the point of

inflection, or with two consecutive tests demonstrating a consistent upward trend.[3]

A small number of patients (18 of the entire group treated or 8 who were observed for more than sixty days) considered to be clinically well could not be classified serologically except as uncertain. Most of these uncertainties were due to technical difficulties, inadequate observations, or failure in agreement of flocculation and complement fixation tests performed simultaneously. In none of these uncertain cases was any tendency toward relapse exhibited, and longer serologic study will be necessary to determine their eventual status.

Clinical together with serologic relapse was encountered five times (2.6 per cent of 191 cases). In none of these infants was there justifiable reason for suspecting reinfection. The following brief protocols indicate the course of events observed.

PROTOCOLS OF CASES

CASE 1.—(U. P. 58) A Negro boy of 4 months received a total dosage of 40,000 units of penicillin per kilogram of body weight; during the next seventy-nine days the serologic titer dropped from 128 to 8 units, but when the infant was next seen, four months later, the eruption had recurred and spirochetes were seen on the dark field; there were severe malnutrition and rise in titer to 64 units. He was given a second course of treatment with a total dosage of 140,000 units per kilogram; clinical results were excellent, with the serum becoming negative at one hundred and sixty-eight days. It has remained so for a total of five hundred and twenty-seven days, dating from the first course.

CASE 2.—(A. 37160) A white boy of 6 weeks received a total dosage of 19,000 units per kilogram of body weight, with rapid healing of visible lesions, and negative serologic reactions at thirty-five and sixty-three days. Clinical and serologic relapse was recognized at ninety-eight days, with a rise in titer to 256 units; osseous lesions had reappeared as well as cutaneous lesions which revealed spirochetes on dark field examination. He was retreated with a total dosage of 36,000 units per kilogram of body weight. Clinical results were again excellent, and following a progressive decline in serologic titer for the next thirty-four weeks, serologic relapse only was recognized at fifty-two weeks. For this second serologic relapse the infant was treated with 41,000 units per kilogram; at the last observation he was clinically well, but the serologic titer was still 256 units.

CASE 3.—(A. 41163) A Negro boy of 11 weeks received a total dosage of 39,000 units per kilogram of body weight, with satisfactory clinical results and decline in serologic titer from 128 to 32 units at six weeks. Serologic relapse at fourteen weeks (256 units) was accompanied by cutaneous syphilids. He was treated again, with a total dosage of 42,000 units per kilogram, and improved clinically. No follow-up studies have yet been made.

CASE 4.—(Tul. 8) A Negro girl of 11 weeks received a total dosage of 20,000 units of penicillin per kilogram of body weight, with uneventful subsidence of clinical manifestations and progressive decline in serologic titer from 280 to 4 units at

3. Minutes of Conference on New Penicillin Forms A and A-1, National Research Council, St. Louis, April 5, 1945.

eighty-one days. Serologic relapse (240 units) was noted at one hundred and eleven days, and this level remained relatively constant over five determinations until clinical relapse occurred at two hundred and seventy days (cutaneous and mucosal lesions revealed spirochetes on dark field examination). She was given a second course of treatment, with a total dosage of 40,000 units per kilogram; the manifestations again subsided, and seven serologic titers during the next two hundred and eighty-eight days have shown a progressive decline to 20 units at the last examination.

CASE 5.—(Tul. 25) A Negro girl of 13 months received a total dosage of 20,000 units per kilogram of body weight, with immediate improvement. The Kahn titer dropped from 360 units to negativity at eight, twenty-five, thirty-two, fifty-three and eighty-eight days. At one hundred and sixteen days, there was serologic relapse (400 units), and by three hundred and twenty-six days the titer had risen to 800 units, with the development of cutaneous syphilids. She was treated again, with a total dosage of 40,000 units per kilogram; the clinical course has been satisfactory, and the serologic titer has slowly declined to 240 units at the last observation, secured one hundred and fifty-six days after the second course of treatment.

Other relapses might have occurred,[4] but these 5 examples are the only ones that have come to our attention during diligent efforts at follow-up studies for 191 infants.

Six infants were given a second treatment with penicillin for reasons other than proved clinical relapse. Observations in this small number do not justify any conclusions regarding the effect of repeated courses of penicillin in treatment of congenital syphilis. The following brief protocols illustrate circumstances justifying a second course of treatment and the effects observed in each case.

CASE 6.—(U. P. 88) This infant was treated again at three hundred and eighty-six days, with double the previous dosage schedule, for persistent seropositivity but no other abnormality; five hundred and nine days after the initial treatment was started and one hundred and twenty-three days after the second course serologic tests for syphilis remained essentially unchanged.

CASE 7.—(U. P. 199) This patient was given a second course of treatment sixty-five days after the first with the same schedule because clinical improvement in associated hydrocephalus was striking following the first course and serologic titer had remained unchanged. Following this, improvement continued, and serologic titer fell to negativity at two hundred and fifty-six days, remaining so to the present (four hundred and nineteen days after initial treatment).

CASE 8.—(U. P. 398) This infant was given a second course of treatment sixty days after the first with no other justification than persistently unchanged positive serologic titer. This fell to negativity one hundred and fifty-five days after the initial course, or ninety-five days after the second course, and is still negative at two hundred and thirty-nine days after initial treatment.

CASE 9.—(Tul. 85) A Negro boy of 6½ months received 40,000 units per kilogram of body weight, with dramatic resolution of florid lesions. One hundred and fifty-six days after this he was seronegative, but two days later he sustained extensive second degree burns. For complicating infections he received sulfadiazine

4. A note concerning further observations is attached to the end of this article.

in conventional dosage, along with sodium penicillin, approximating 110,000 units per kilogram over a period of twelve days, almost three times the amount which had apparently cured his syphilis five months earlier. Eleven days after the burn, the Kahn titer was 20 units, and one hundred and thirty-five days later, or two hundred and ninety-three days after the initial course, he was clinically well and seronegative.

CASE 10.—(A. 3437) A white girl 7 weeks old received 16,000 units per kilogram, with clinical improvement and progressive decline in serologic titer from 256 to 64 units at two hundred and seventy-three days. She was then given a second course of treatment with 43,000 units per kilogram because of persistence of malnutrition and osseous lesions. Again there was improvement, gain in weight and further progressive decline in serologic titer, to 4 units at seventy-two and eighty weeks after the original course.

CASE 11.—(A. 38338) A white girl 12 weeks old received 46,000 units per kilogram of body weight, with rapid healing of all lesions. A serologic titer of 16 units before treatment rose to 64 units two weeks later, then declined to 8 units at four weeks and negativity at six weeks; it then rose progressively from 2 units at ten weeks to 32 units at fifteen weeks, 64 units at twenty-six weeks and 256 units at thirty-one weeks. The cerebrospinal fluid was unchanged (group II), but no true evidences of clinical relapse were noted. She was given a second course of treatment with 32,000 units per kilogram, and the serologic titer eleven weeks later (forty-five weeks after the first course) was 128 units.

When results are considered in relation to dosage of penicillin employed, there are apparent differences in favor of schedules comprising 40,000 units or more per kilogram of body weight. Table 3 classifies results as satisfactory, unsatisfactory or uncertain in relation to total dosage of penicillin employed for infants observed more than sixty days after treatment. A satisfactory result implies apparent clinical cure with subsidence of lesions attributable to syphilis, together with a negative or progressively declining serologic titer. An unsatisfactory classification indicates persistence of lesions attributable to syphilis, accompanied by stationary or rising serologic titer; there may be evidences of clinical or serologic relapse as well. Results for 8 infants had to be classed as uncertain because of inadequate observations or because enough time has not elapsed to insure classification in either of the other two categories.

Most of these infants were treated with dosage schedules of 20,000 40,000, 60,000 or 80,000 units per kilogram calculated on the basis of actual body weight at the time treatment was started; occasionally treatment schedules were irregular so that expressed ranges were necessary for purposes of tabulation.

Though sufficient time has not elapsed for satisfactory comparison of patients treated most recently with larger dosage schedules and though differences may be explained in part by selection of cases or by variation in constituents of various lots of penicillin, this analysis indicates that satisfactory results were secured in almost 90 per cent of infants treated with 40,000 units or more per kilogram of body weight as

contrasted with 74 per cent with the smaller dosage schedules. Some of the infants most recently treated with 80,000 units or more per kilogram have received this amount of the drug divided into one hundred and twenty equal injections given at three hour intervals over a period of fifteen days. This increase in the total number of injections and consequent prolongation of therapy, designed to improve our results, cannot yet be evaluated.

DEATHS

Table 4 includes pertinent observations regarding 24 infants who died during or after a prescribed course of treatment with penicillin. In one of the cooperating clinics (Johns Hopkins), there were 7 such deaths among 55 infants treated with arsenicals and heavy metals just before this present study was initiated [5]; thus, the percentage of deaths occurring under roughly comparable circumstances were almost identical in these two groups: 12.58 per cent among 191 patients treated with penicillin and 12.72 per cent among 55 treated just previously by conventional means.

Five deaths occurred during therapy, but none of these could be attributed to penicillin, the particular plans of treatment employed or therapeutic shock. Most of these infants had immediate causes of death more obvious than syphilis: bronchopneumonia, acute nutritional disturbances, purulent otitis media, prematurity, congenital cardiac defects, septicemia, sickle cell disease, purulent pericarditis or septic thrombophlebitis. In 3 infants who died at home, no accurate conclusion as to cause of death could be reached.

Necropsies were performed on 10 of the 24 dead infants, and in only 5 of these did pathologists note lesions attributable to syphilis; it is important to note that these 5 instances were encountered among 10 infants dying within twenty-six days after treatment with penicillin had been initiated. Though other adequate causes of death were noted when there was opportunity for clinical or pathologic study, syphilis obviously must be considered as at least a contributory factor in each case.

In one of the cooperating clinics (Johns Hopkins), 5 of the 10 deaths were considered to be sudden and unexpected. Although there was concern that these might possibly have been related to the administration of penicillin, careful review of each case indicated other causes in themselves adequate to explain death. Because these 5 fatalities were the only ones for which penicillin was considered to be a contributory factor, brief summaries are included.

One of these occurred in a feeble infant of 5 weeks (A. 39673) forty-five hours after treatment with penicillin had been started. She

5. Goodwin, M. S.: Personal communictaion to the authors.

TABLE 4.—*Deaths in Infants with Early Congenital Syphilis*

Case No.	Age at Start *	Serologic Titer at Start (R. U.)	Clinical Severity at Start	Total Dosage Penicillin, U./Kg.	Age at Death *	Serologic Titer Up to Last Observation	Clinical Evidence of Syphilis at Last Observation	Apparent Cause of Death (Observed or Reported)	Autopsy
Tul. 4	79	0; Kline, Kolmer +	III	20,000	106	?	Improved	Convulsions, hepatitis, acute nutritional disturbance	Bronchopneumonia, lung abscesses, atelectasis; splenomegaly, jaundice, "compatible with congenital syphilis"
Tul. 55	138	400	III	40,000	147	Decreased; 120 u. at 9 days	No change	Acute nutritional disturbance	Not done
Tul. 131	32	1,600	IV	40,000	45	Decreased; 800 u. at 13 days	Improved	Bronchopneumonia; acute nutritional disturbance	Bronchopneumonia; congenital syphilis
Tul. 100	6 mo.	160	III	40,000	9 mo.	Increased; 400 u. at 55 days	Improved	Bronchopneumonia; acute nutritional disturbance	Not done
Tul. 92	66	480	IV	20,000	210	Negative at 142 days	Improved	Acute nutritional disturbance (died at home)	Not done
Tul. 153	16	2,000	IV	80,000	57	Decreased; 200 u. at 11 days	Improved	No data; died at home	Not done
J. H. A. 40844	10	64	IV	40,000	55	Increased; 128 u. at 52 days	Improved	Progressive jaundice; acute nutritional disturbance	Not done
J. H. A. 40214	2 mo.	256	III	40,000	4¾ mo.	Decreased; 32 u. at 63 days	Improved	Acute nutritional disturbance	Not done
J. H. A. 36165	86	32	II	17,000	6 mo.	Decreased; 4 u. at 14 weeks (then relapse: 64 u.)	Improved	Acute nutritional disturbance; sickle cell anemia	Not done
J. H. A. 39081	5½ mo.	256	II	44,000	9 mo.	Decreased; 128 u. at 81 days	Improved	Acute nutritional disturbance	Not done
J. H. A. 38575	39	0 (Wass. s. c.)	III	37,000	2 mo.	Not observed	Improved	Pneumonia	Type VI pneumonia and pleurisy; extensive extramedullary hemopoiesis

J. H. A. 39673	34	12	I	1,200	36	Not observed	None	Acute nutritional disturbance; secondary anemia, anasarca, prematurity	Ascites, hydrothorax, pericardial effusion
J. H. A. 34599	189	128	II	100,000	201	No change at 12 days	Improved	Thrombophlebitis; acute nutritional disturbance; otitis media	Not done
J. H. A. 42284	114	512	III	45,000	125	Decreased; 256 u. at 12 days	Improved	Acute nutritional disturbance; otitis media	Pneumonia alba; generalized adenopathy, hepatosplenomegaly; Staphylococcus aureus from cerebrospinal fluid
J. H. A. 42649	98	256	III	40,000	107	Not observed	Improved	Acute nutritional disturbance; large subcutaneous abscess	Not done
J. H. A. 41662	46	256	III	40,000	66	Decreased; 32 u. at 18 days	Improved	Septicemia (pyocyaneus); sickle cell anemia; otitis media	Purulent pericarditis (Pseudomonas aeruginosa); splenomegaly
U. P. 507	31	128	III	79,904	2 mo.	No change; 128 u. at 12 days	Improved	Malnutrition	Not done
U. P. 112	57	128	III	23,388	2 mo.	Decreased; 64 u. at 8 days	Worse	Parenteral infection; dehydration, diarrhea; aspiration of food	Aspiration of food; congenital syphilis
U. P. 286	41	32	IV	620	42	Not observed	Worse	Bronchopneumonia; malnutrition; severe anemia	Bronchopneumonia; congenital syphilis; anemia
U. P. 299	46	32	II	135,388	19 wk.	Decreased; 2 u. at 84 days	None	Severe fulminating respiratory infection	Not done
U. P. 397	96	?	II	54,641	4 mo.	Not observed	No change	Bronchopneumonia; Staph. septicemia; otitis media; congenital syphilis	Not done
U. P. 47	19	128	III	39,818	5 wk.	No change at 17 days	No change	Pneumonia; cardiac failure; diarrhea; congenital syphilis	Not done
U. P. 552	76	256	III	81,133	3 mo.	Decreased; 128 u. at 7 days	No change	Aspiration of vomitus; anemia; diarrhea	Bronchial obstruction; congenital syphilis
Tex. 1181B	69	128	II	38,600	8 mo.	Decreased	Healed	Cerebral edema after operation for craniostenosis	Operative death; no evidence of syphilis

* Ages are given in days unless otherwise indicated.

died immediately after intravenous administration of dextrose and plasma given for a complicating acute nutritional disturbance; autopsy revealed edema, ascites, bilateral hydrothorax and pericardial effusion.

The second, a Negro girl of 6 weeks (A. 41662), died with acute gastrointestinal symptoms twelve days after a prescribed course of 40,000 units per kilogram had been completed. Improvement in syphilitic manifestations had been recorded; autopsy revealed fibrinopurulent pericarditis.

The third, a Negro boy of 18 months (A. 34599), died suddenly thirty-eight hours after completion of a prescribed course of approximately 40,000 units per kilogram. No autopsy was done, though there was extensive cellulitis and saphenous thrombophlebitis attributed to the recent continuous intravenous administration of fluids for treatment of intercurrent severe diarrhea and dehydration.

The fourth patient, a white boy of 12 weeks (A. 42649), died suddenly twenty hours after receiving the last prescribed injection of penicillin. Clinical evidences of syphilis had improved, though there was a large sloughing area over the back at the site of eariler subcutaneous administration of fluids, and severe diarrhea had developed during the administration of penicillin. No bacteriologic data or autopsy report were available.

The fifth infant (A. 42649), a white boy of 4 months, died suddenly two days after completion of a prescribed course of penicillin, although external evidences of syphilis were much improved. On the last day of treatment bilateral otitis media and persistent, severe diarrhea developed. He died two hours after intravenous administration of fluids; hemolytic Staphylococcus aureus was recovered from the cerebrospinal fluid at autopsy, which also showed lesions attributable to congenital syphilis.

From a review of the data available for all 24 infants who died during and after treatment, it was determined that clinical evidences of syphilis had improved or disappeared in 18, no change was observed in 4, and the manifestations were apparently aggravated in 2. Other causes, at least contributory to death, were demonstrated clinically or pathologically in each case in which there was opportunity for study. Serologic titers had decreased or become negative in 13, had remained stationary in 3, increased in 2 and could not be evaluated in 6 because of inadequate observations.

CHANGES IN THE CEREBROSPINAL FLUID

Because the significance of abnormal spinal fluid in early congenital syphilis is not entirely clear, it would not be fair to compare these changes with those in adults following penicillin therapy. There has,

however, been a striking change observed in abnormalities of the spinal fluid; these were classified according to the recommendations of the cooperative clinic group[6]:

Group I: There is an increase in cells and/or protein and the Wassermann and colloidal reactions are negative (the Wassermann reaction is negative with a minimum of 1 cc. of fluid, and the colloidal test shows no tube reading higher than 2).

Group II: Any fluid with a positive Wassermann reaction in any amount which does not fit into Group III is placed in this group.

Group III: The paretic formula. Cells and protein are usually increased, the Wassermann reaction strongly positive (0.2 cc. or smaller amounts), colloidal test zone 1, or paretic in type.

Unclassified: A small number of fluids which fail to fit into group I are unclassified because results of the colloidal test are abnormal.

TABLE 5.—*Changes in the Cerebrospinal Fluids Recorded After Penicillin Therapy in Early Manifest Congenital Syphilis* *

Before Treatment, Grade	Total	After Treatment, Grade			
		0	I	II	III
0	17	17	..	..	..
I	16	13	2	1	..
II	23	15	4	4	..
III	8	3	3	1	1†
Total	64	48	9	6	1

* Initial examinations of the cerebrospinal fluid were made just before treatment was started; follow-up examinations were secured at intervals of eight days to fifteen months after the date of starting but usually include those made after six months.
† At three weeks.

The data included in table 5 were compiled from 64 cases in which observations were made both before and after treatment; follow-up examinations were secured at intervals of eight days to fifteen months after the date of initiating therapy, though efforts were generally made to secure these at approximately six months. Only 4 of these infants had clinical manifestations attributable to syphilis of the central nervous system, and these all improved remarkably.

SUMMARY AND CONCLUSIONS

Though the best method for its use has not been defined, penicillin appears to be the best single agent for the treatment of infantile congenital syphilis. The total dosages employed for effective treatment have varied from 20,000 up to 150,000 units per kilogram of body weight among infants for whom adequate observations have been made. It is recommended that dosage schedules in excess of 40,000 units per

6. Moore, J. E.: The Modern Treatment of Syphilis, Springfield, Ill., Charles C Thomas, Publisher, 1943, p. 352.

kilogram be used, and that treatment continue for 60 or more equal intramuscular injections given at three hour intervals. Schedules comprising 80,000 or more units per kilogram, divided into 120 equal intramuscular injections given every three hours night and day for a period of fifteen days, have not yet been evaluated.

Reactions to therapy have appeared unimportant, and we have seen no justification for gradually increasing dosage at the outset of a projected course to avoid these.

Only a relatively small number of infants will demonstrate seronegativity during or soon after a single course of penicillin. The number of patients becoming seronegative increases with each month of observation for at least eighteen months. Careful periodic examinations are necessary to recognize the small number of serologic and clinical relapses which will require additional therapy.

Deaths among infants included in this series do not appear to be related to the use of penicillin or to therapeutic shock.

Final evaluation of the efficacy of penicillin in congenital syphilis must await trial of additional schedules of treatment and methods of administering the drug, as well as clarification of the relative spirochetocidal and spirochetostatic action of its constituent fractions.

NOTE.—Since this paper was prepared, further observations over an additional five months have not disclosed any additional examples of relapse in infants followed more than one year after treatment. Because of the changing character of penicillin mixtures, we have recommended a total dosage of at least 100,000 units of penicillin per kilogram of body weight, divided into approximately one hundred and twenty equal intramuscular injections, given at intervals of no longer than three hours "around the clock" for a period of twelve to fifteen days (Platou, R. V., and others: Early Congenital Syphilis: Treatment of Two Hundred and Fifty-Two Patients with Penicillin, J. A. M. A., to be published).

PARENTERAL ADMINISTRATION OF AMMONIUM CHLORIDE FOR ALKALOSIS OF CONGENITAL HYPERTROPHIC PYLORIC STENOSIS

A Preliminary Report

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IN A RECENT review [1] of the cases of congenital hypertrophic pyloric stenosis seen at the St. Louis Children's Hospital during the past twelve years, emphasis was placed on the proper preoperative preparation of the patient for the attainment of normal fluid and acid-base equilibriums. In the majority of patients these particular objectives can be satisfactorily realized by the administration of dextrose and isotonic solution of sodium chloride or isotonic solution of three chlorides U. S. P. (Ringer's solution). If sufficient water and electrolyte are given, a satisfactory adjustment can then be accomplished through renal activity. The relief of alkalosis by this means is at best a rather slow process, often requiring two or three or more days for its completion. Moreover, the entire process depends wholly on the renal function of the patient. If renal activity is impaired by persistence of anhydremia due to low plasma proteins or by preexisting renal disease, alkalosis may actually be entirely unaffected.

In the series just referred to, 3 patients suffered such extreme alkalosis that, despite vigorous parenteral fluid therapy, death occurred before they could be prepared for operation. Further, on 2 occasions severe and near-fatal reactions were witnessed directly following pyloroplasty in patients whose alkalosis and hypochloridemia had not been adequately corrected. It is well known that severe alkalosis can result in generalized convulsions and in fatal depression of respiration in the small infant. In the past such emergencies have been treated, not always successfully, by the inhalation of carbon dioxide and oxygen, intravenous administration of calcium chloride and the use of various respiratory stimulants. As a last resort, hydrochloric acid was given intravenously to 4 patients in concentrations ranging from one-half molar to one-seventeenth molar. Three of these patients obtained

From the Department of Pediatrics, Washington University School of Medicine, and the St. Louis Children's Hospital.

1. Akin, J. T., Jr., and Forbes, G. B.: Congenital Hypertrophic Pyloric Stenosis, Surgery, to be published.

prompt and gratifying relief of symptoms. Since hydrochloric acid is an extremely strong acid, it must be given intravenously, and the utmost caution must be used to avoid disastrous overdosage. It also has the disadvantage of being extremely irritating to the walls of veins near the site of the injection.

In an effort to improve preoperative preparation of these patients, thought was given to the possibility of using some other agent for the control of severe alkalosis, the action of which would be independent of renal activity. Prompted by the report of Zintel, Rhoads and Ravdin,[2] we began a study of the parenteral administration of ammonium chloride for the correction of severe alkalosis of the metabolic type.

The action of ammonium chloride depends on the rapid conversion of the ammonium radical to urea by the liver, with the release of chloride for combination with the fixed base of the body fluids. The conversion of ammonia to urea goes almost to completion in the perfused liver, and it does not seem to be hampered even by hepatic damage of the type produced by chloroform and phosphorus.[3] There is some doubt that an increase in the ammonia content of the systemic circulation has ever been detected, even after ingestion of large amounts of ammonium salts or in circumstances which enormously increase the urinary ammonia content.[4] It is a well established fact that the ammonia which appears in the urine following the administration of ammonium chloride is formed in the tubules of the kidney by deamination of certain amino acids for the purpose of conserving the fixed base of the body and does not represent that which was originally given.

The early work of Gamble [5] and of Haden and Orr [6] clearly demonstrated that isotonic solution of sodium chloride was effective in prolonging the life of animals with experimental pyloric stenosis, and Hartmann [7] was the first to use lactate-Ringer solution [8] for a similar

2. Zintel, H. A.; Rhoads, J. E., and Ravdin, I. S.: The Use of Intravenous Ammonium Chloride in the Treatment of Alkalosis, Surgery **14**:728 (Nov.) 1943.

3. Fiske, C. H., and Karsner, H. T.: The Effect of Acute Destructive Lesions of the Liver on Its Efficiency in the Reduction of the Ammonia Content of the Blood, J. Biol. Chem. **18**:381, 1914.

4. Peters, J. P., and Van Slyke, D. D.: Quantitative Clinical Chemistry, Baltimore, Williams & Wilkins Company, 1931, vol. 1.

5. Gamble, J. L., and Ross, S. G.: The Factors in the Dehydration Following Pyloric Obstruction, J. Clin. Investigation **1**:403 (June) 1925.

6. Haden, R. L., and Orr, T. G.: The Effect of Inorganic Salts on the Chemical Changes in the Blood of the Dog After Obstruction of the Duodenum, J. Exper. Med. **39**:321 (Feb.) 1924.

7. Hartmann, A. F., and Elman, R.: The Effects of Loss of Gastric and Pancreatic Secretions and the Methods for Restoration of Normal Conditions in the Body, J. Exper. Med. **50**:387 (Sept.) 1929.

8. A mixture of 1 part of 1 molar sodium-r-lactate and 40 parts of hypotonic Ringer solution.

purpose. The former workers also showed that parenterally administered ammonium chloride did not prolong the life of these animals as did sodium chloride for the reason, as Gamble [5] indicated, that the vomitus in cases of pyloric obstruction contains an appreciable amount of sodium in addition to a large quantity of chloride. Thus these patients may suffer an actual depletion of body sodium with a resultant decrease in total serum electrolyte. As a consequence of the diminution of the serum total "fixed" base, a great many children with alkalosis the result of pyloric obstruction will excrete an acid urine because of compensatory tubular reabsorption of sodium bicarbonate.[9] In such cases it is evident, then, that the body stores of sodium as well as of chloride must be replenished if fluid and acid-base equilibriums are to be restored.

For the patients herein reported, we have employed a solution which contains both ammonium and sodium chloride. The solution is made up by adding dry ammonium chloride ("analytic grade") to isotonic solution of sodium chloride or isotonic solution of three chlorides U. S. P. (Ringer's solution) in an amount sufficient to make a one-sixth molar solution of the ammonium salt (8.9 Gm. of ammonium chloride per liter). This solution is autoclaved in the usual manner at a pressure of 15 pounds (6.8 Kg.) for thirty minutes and is then ready for use. It has a p_H of 5.2, is colorless and is stable over a period of at least several months. It has practically no titratable acidity, as the addition of only 0.4 cc. of one-tenth normal sodium hydroxide to 100 cc. of the solution will raise the p_H to 7.0.

Preliminary experiments on dogs and rabbits revealed that this solution did not irritate the subcutaneous tissues. The intravenous injection of 20 to 30 cc. per kilogram of body weight in dogs produced excessive salivation, hyperpnea and drowsiness but no other symptoms of importance when the injection was made over a period of forty-five minutes. Speeding up the rate of injection produced stupor and convulsions. It was noted that the symptoms produced in each experiment were directly related to the rate of injection of the solution. Although each dog suffered a profound acidosis (serum p_H values and carbon dioxide contents of the order of 7.0 and 20 volumes per cent respectively) as a result of the injection, it was found that pronounced hyperpnea and other symptoms such as retching occurred only when the solution was injected rapidly and that breathing became much more normal when the rate of injection was slowed. Recovery from acidosis was practically complete eight hours after the administration of ammonium chloride.

9. Hartmann, A. F., and Smyth, F. S.: Chemical Changes in the Body Occurring as the Result of Vomiting, Am. J. Dis. Child. **32**:1 (July) 1926.

CLINICAL RESULTS

In order to gain experience with the use of this therapeutic agent, we gave it to every patient with congenital hypertrophic pyloric stenosis who presented a significant elevation of serum bicarbonate, and this report represents our experiences with 9 such infants treated during the past twelve months. Chemical analyses of the blood were done for each patient before and after the administration of the ammonium chloride, and the infants were carefully observed for evidences of clinical toxicity. All samples of blood were obtained from the femoral vein, the blood being placed immediately under oil. In the charts to follow, "CO_2" indicates carbon dioxide content of the serum in volumes per cent, determined by the method of Van Slyke and Neill;[10] serum p_H was measured by the bicolor method of Hastings and Sendroy;[11] "Cl" refers to serum chloride, as sodium chloride, in milligrams per hundred cubic centimeters measured by the method of Van Slyke and Sendroy;[12] and nonprotein nitrogen values are expressed as milligrams per cent of nonprotein nitrogen, as measured by the micro-Kjeldahl method and direct nesslerization after precipitation of the serum proteins with trichloroacetc acid. Because of the difficulties in collecting urine samples suitable for the analysis of p_H and carbon dioxide content from most of the patients, a sufficient number of accurate studies of the urine on which to base definite conclusions are not available at this date.

In order to contrast the usual methods for the relief of alkalosis due to pyloric obstruction with those employing ammonium chloride, the following case from the files of the St. Louis Children's Hospital is presented as a fairly representative example (chart 1). This patient, whose case has been reported by Hartmann,[13] was dehydrated and severely alkalotic on admission to the hospital. The infant's respirations became normal only after forty-eight hours of parenteral fluid therapy. Even though complete acid-base equilibrium had not been achieved, a successful Fredet-Ramstedt pyloroplasty was done; vomiting promptly ceased, and the patient's convalesence was uneventful. The slowness with which alkalosis is brought under control with the commonly employed solutions (dextrose, isotonic solution of sodium chloride,

10. Van Slyke, D. D., and Neill, J. M.: The Determination of Gases in Blood and Other Solutions by Vacuum Extraction and Manometric Measurement: I., J. Biol. Chem. **61**:523 (Sept.) 1924.

11. Hastings, A. B., and Sendroy, J., Jr.: Studies of Acidosis: XX. The Colorimetric Determination of Blood p_H at Body Temperature Without Buffer Standards, J. Biol. Chem. **61**:695 (Oct.) 1924.

12. Van Slyke, D. D., and Sendroy, J., Jr.: The Determination of Chloride in Blood and Tissues, J. Biol. Chem. **58**:523 (Dec.) 1923.

13. Hartmann, A. F.: Notes on Parenteral Fluid Administration, St. Louis, Washington University School of Medicine, Department of Pediatrics, 1940.

and isotonic solution of three chlorides U. S. P.) has doubtless resulted in many pyloroplasties being done before conditions were optimal with respect to acid-base equilibrium.

The next three charts are illustrative of effects of parenterally administered ammonium chloride. Chart 2 presents a patient whose clinical status on admission to the hospital was roughly comparable to that depicted in chart 1. Shortly after admission, 30 cc. per kilogram of one-sixth molar ammonium chloride in isotonic solution of sodium chloride was given intravenously over a period of thirty minutes. There were no untoward effects from the injection. As the chart indicates, injections of isotonic solution of three chlorides U. S. P. and dextrose

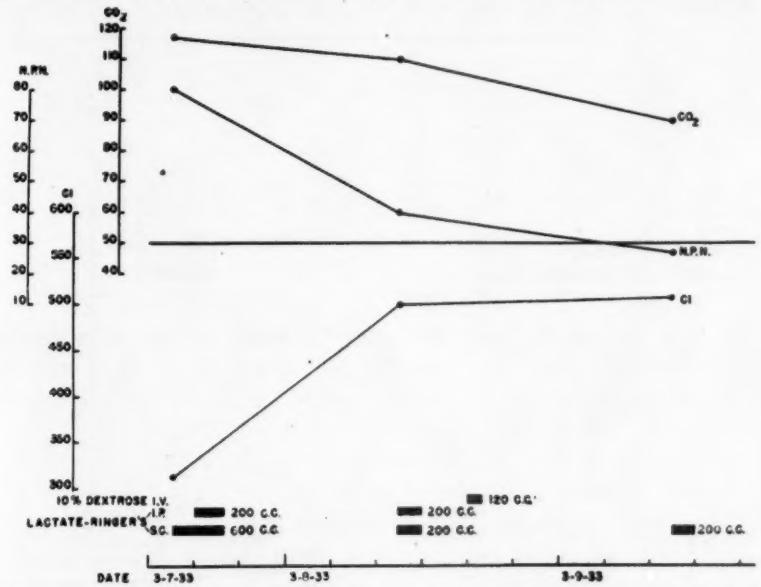

Fig. 1.—R. M., weight 4.2 Kg. Results of the usual methods for the relief of alkalosis due to pyloric obstruction.

solutions were given later. It is evident that the response of serum bicarbonate, p_H and chloride is most prompt, significant changes occurring within a matter of minutes, rather than days, as illustrated in chart 1. The nonprotein nitrogen value, elevated as a result of dehydration and oliguria, rose slightly as a result of the injection and then fell progressively as body hydration and diuresis were established.

Chart 3 represents an infant who exhibited a pronounced degree of dehydration and clinical alkalosis on admission to the hospital. Three hours after the administration of dextrose solution intravenously and isotonic solution of three chlorides U. S. P. subcutaneously, his state of hydration was improved and his color better, but he continued to show

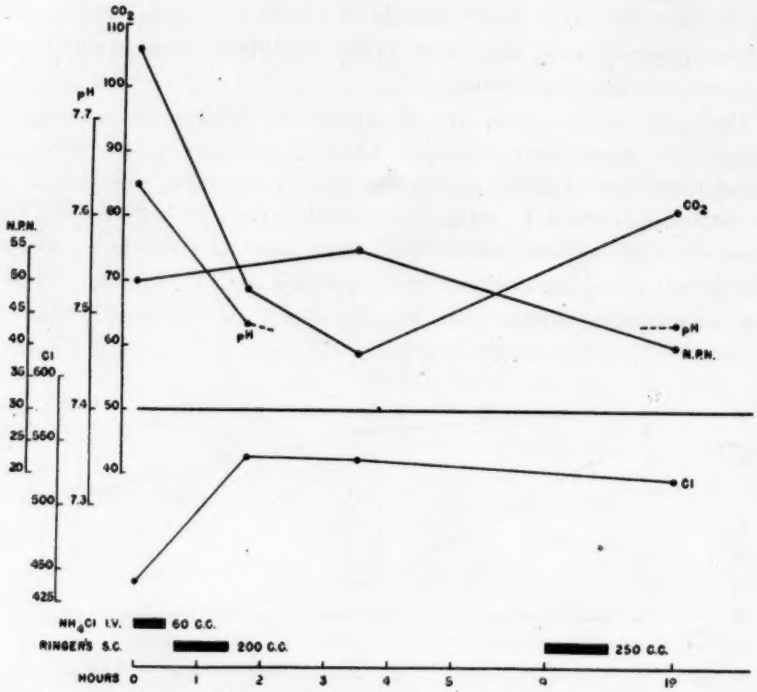

Fig. 2.—J. M., weight 2,200 Gm. (Aug. 6, 1945). Effects of ammonium chloride given intravenously.

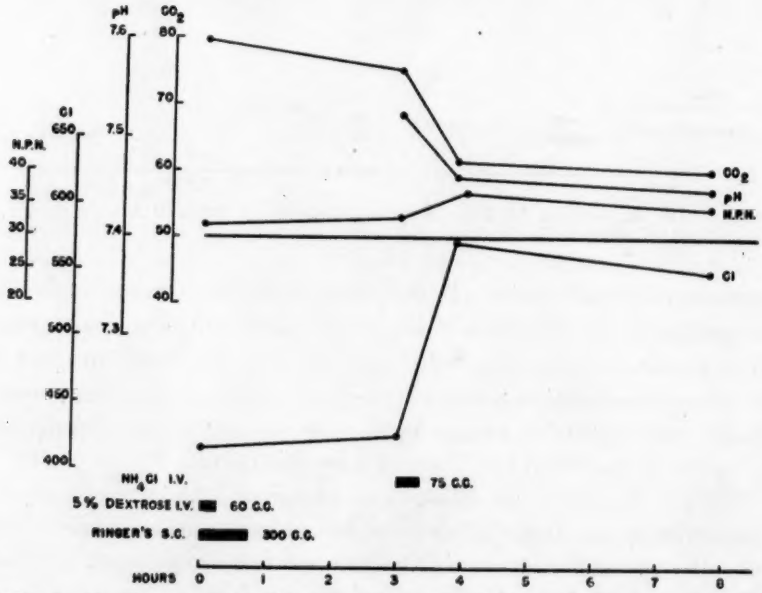

Fig. 3.—D. R., weight 3,610 Gm. (May 29, 1945). Effects of ammonium chloride given intravenously.

both clinical and chemical evidence of alkalosis. Twenty cubic centimeters per kilogram of one-sixth molar ammonium chloride in isotonic solution of sodium chloride was then given intravenously over a period of twenty-three minutes. There was no reaction to the injection. The chart illustrates well the prompt reduction of serum bicarbonate and p_H and the elevation of serum chloride which took place following this injection. Here, too, a transient rise in serum nonprotein nitrogen occurred.

Chart 4 illustrates the sequence of events following the subcutaneous infusion of 30 cc. per kilogram of one-sixth molar ammonium chloride in isotonic solution of three chlorides U. S. P. The patient had mild clinical alkalosis at the time. The infusion was made in the subcutaneous tissues

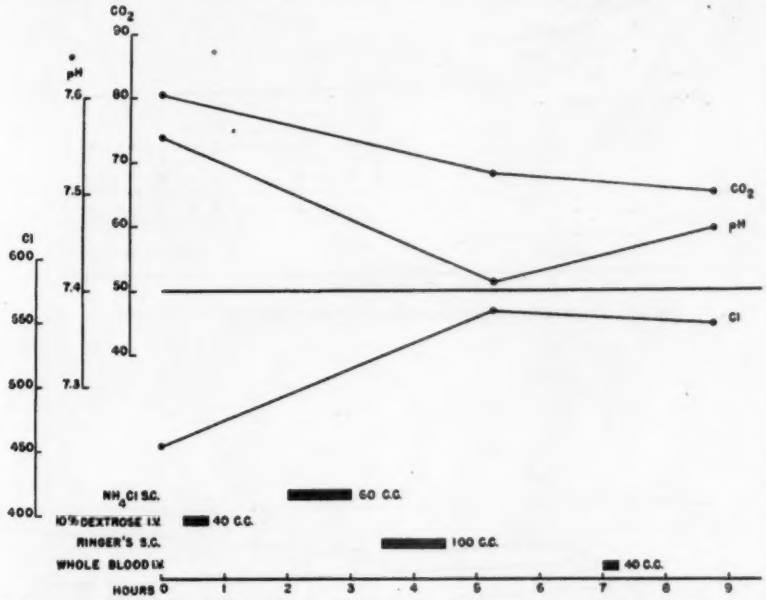

Fig. 4.—R. N., weight 2,000 Gm. (Dec. 5, 1945). Effects of ammonium chloride given subcutaneously.

of the thigh and was allowed to run in by gravity. About four hours was required for complete absorption of the fluid. There was no evidence of tissue reaction at the site of the infusion. The resultant changes in serum bicarbonate, p_H and chloride were about as great as those produced by intravenous injection, but they occurred more slowly.

In charts 5, 6, and 7 the changes in serum bicarbonate, chloride and p_H respectively are plotted for each of the 9 patients in this series, the dose in cubic centimeters of one-sixth molar ammonium chloride solution per kilogram used in each case being indicated in the accompanying legends. The solid curves represent results for those patients who

received the solution intravenously, and the dotted ones represent the results for those who received it subcutaneously. A definite reduction of serum bicarbonate and an elevation of serum chloride were observed for each of the 9 patients, and the p_H of the serum was lowered in

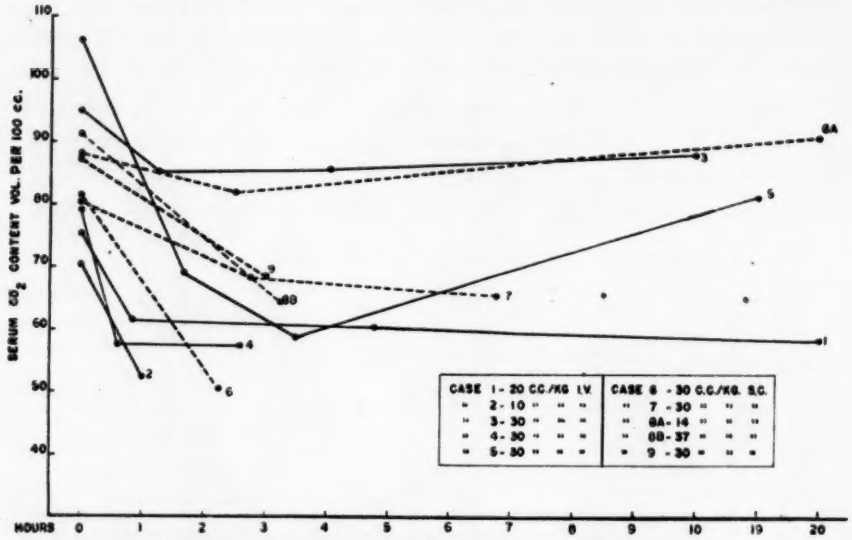

Fig. 5—Changes in serum bicarbonate in each of 9 cases.

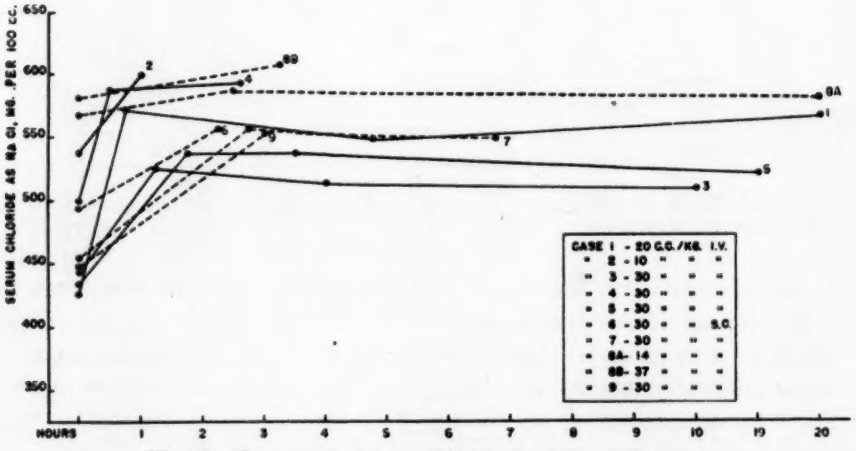

Fig. 6.—Changes in serum chloride in each of 9 cases.

each of the 7 patients for whom we have determinations of the serum p_H. Patient 8 received a second injection (see case 8 B) on the day following the first injection, since the latter was obviously inadequate.

The hope that a fairly good correlation could be shown between the dose of ammonium chloride employed and the resultant drop in the serum bicarbonate has not been realized.[14] The lowering of the serum bicarbonate that was observed ranged from 0.33 to 1.77 volumes per cent, with an average of 0.88 volumes per cent, for each cubic centimeter of one-sixth molar ammonium chloride solution given per kilogram of body weight. The explanation for the fact that the average drop in serum bicarbonate is somewhat greater than would be anticipated on theoretic grounds is not yet clear. One possible explanation would be that since the injected ammonium chloride is made rapidly available

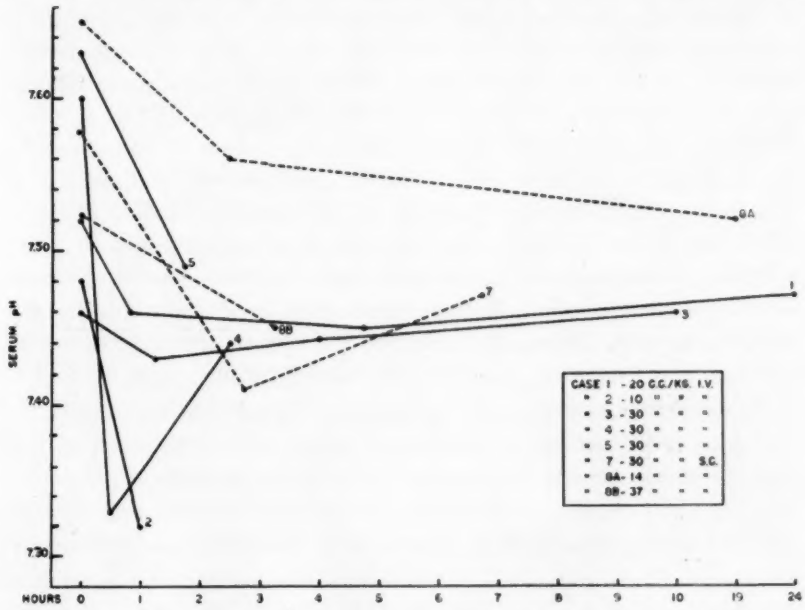

Fig. 7.—Changes in p_H in each of 9 cases.

throughout blood plasma and extracellular fluid for combination with bicarbonate, changes occur in those fluid compartments first, and only after complete distribution of these changes throughout the entire body

14. The theoretic drop in serum bicarbonate which should occur following the administration of 1 cc. per kilogram of body weight of a one-sixth molar solution of ammonium chloride can be calculated as follows: Assuming that two thirds of the body weight is water, the administration of this amount of ammonium chloride will displace ½ cc. of one-sixth molar sodium bicarbonate per liter of body fluid. Since ½ cc. of one-sixth molar sodium bicarbonate will liberate $\frac{3}{2} \times \frac{22.4}{6}$ cc., or 5.6 cc., of carbon dioxide, the use of this amount of ammonium chloride should reduce the carbon dioxide content of the serum by 0.56 volumes per cent.

fluids do the final effects become apparent. This is suggested by the results illustrated in chart 2, in which the serum bicarbonate after an initial precipitous drop slowly rose again after several hours had elapsed. At the present stage of our experiments, then, it is impossible to advocate a specific dose of ammonium chloride for any given patient.

TOXICITY

One of our purposes in giving this solution to as many patients as possible was to test the toxicity of the material in human beings. The information available in the standard pharmacology texts on the toxicity of parenterally administered ammonium chloride is not clear as to whether the observed symptoms (drowsiness, irregular respirations, convulsions and others) are due to a direct toxic effect of the ammonium radical or to the extreme acidosis produced. One investigator reported the use of intravenously administered ammonium chloride (10 cc. of a 5 per cent solution injected rapidly) for the induction of convulsions in the treatment of schizophrenia.[15] By this means a generalized convulsion lasting fifteen to thirty seconds was produced, from the effects of which the patient usually completely recovered within fifteen to thirty minutes. Zintel and his co-workers [2] gave twelve separate injections of a 2 per cent solution of ammonium chloride to 7 patients by slow intravenous drip. The only reactions which they encountered were 3 instances of scintillating scotomas and 1 of mild chill.

It is well known that the ammonium radical diffuses readily into red blood cells, with the production of hemolysis. Preliminary in vitro tests, in which varying amounts of one-sixth molar ammonium chloride solution and isotonic solution of sodium chloride were mixed in such a way that the resultant solution was isotonic, revealed that concentrations of ammonium chloride of one-fifteenth molar or greater readily produced hemolysis of human red blood cells. However, we have observed neither clinical icterus nor evidence of hemolysis in the samples of blood of any of our patients. Repeated samples of urine from 2 patients following the administration of ammonium chloride gave negative reactions to tests for urobilinogen.

There were no local effects observed after intravenous or subcutaneous injection of the solution of ammonium chloride and the infants appeared to suffer no more pain than that seen after the injection of isotonic solution of three chlorides U. S. P. (Ringer's solution). In view of Gamble's report [5] of intense irritation following the intraperitoneal administration of solutions of ammonium chloride we have been reluctant to employ this route of administration in infants.

15. Rizvi, K. N. H., and Lucknow, B. S.: The Ammonium Chloride Treatment of Schizophrenia, J. Ment. Sc. **88**:575 (Oct.) 1942.

General reactions have been few. Those patients who had clinical alkalosis at the time of the injection usually improved considerably in their general appearance and color and in the character of their respirations. One patient had transient pallor but no other symptoms. In only 1 patient did we observe definitive toxic effects. The baby (case 4, charts 5, 6 and 7) weighed 2,650 Gm., was well hydrated and presented mild symptoms of clinical alkalosis. He was given 30 cc. per kilogram of one-sixth molar ammonium chloride in isotonic solution of sodium chloride intravenously over a period of eighteen minutes, with a resultant drop of the serum carbon dioxide content from 79 to 57 volumes per cent and of serum p_H from 7.60 to 7.33. At the completion of the injection he became pale, breathed irregularly and had occasional twitchings of the eyelids and hands, bradycardia (75 beats per minute) and poor response to painful stimuli. Without treatment he recovered completely within a few minutes except for some tendency toward drowsiness. Within an hour he seemed normal in all respects, and a sample of blood two hours after the injection showed the serum carbon dioxide content to be 57 volumes per cent and the serum p_H to be 7.44. We believe that this patient's reaction was probably caused by the too rapid injection of the solution, with the production of an extensive fall in serum p_H. Once the effect of the solution had been dissipated throughout the body fluids, the serum p_H rose slightly and the toxic effects disappeared. Since the reaction was much the same as that which we had observed in normal animals following the use of ammonium chloride, this interpretation of what happened in this patient seems justified.

In view of the fact that the ammonium radical is converted to urea in the body, we were not surprised to observe transient elevations of serum nonprotein nitrogen values in our patients. For the 5 patients in whom we have such observations, the rise in serum nonprotein nitrogen ranged from 1.6 to 6.0 mg. per hundred cubic centimeters in 4, while 1 showed no rise whatsoever. The latter patient had a value for serum nonprotein nitrogen of 121 mg. per hundred cubic centimeters prior to the injection and values of 121 and 108 mg. one and four hours, respectively, following it. There should be no reason to withhold parenteral therapy with ammonium chloride for patients with azotemia.

COMMENT

We feel that parenterally administered ammonium chloride will prove to be a useful adjunct in the therapy of alkalosis of the metabolic type. It is an extremely effective agent for the reduction of serum bicarbonate and p_H and for the elevation of serum chloride. Its action

is independent of renal processes, and its toxicity is seemingly low when it is properly given. It apparently does not irritate the subcutaneous tissues or the blood vessel walls, and thus can be given either intravenously or subcutaneously. There are, however, four important considerations which should be borne in mind in regard to its clinical use.

First, in the treatment of alkalosis due to pyloric obstruction, care should be taken to combine the ammonium chloride with some solution containing sodium, such as isotonic solution of sodium chloride or isotonic solution of three chlorides U. S. P. If this is not done, lasting benefit to the patient will not occur, and there is even risk of further dehydrating the patient.[5]

Second, the other important aspects of the preoperative treatment of patients with pyloric stenosis should not be overlooked. The patient will still need to be given large amounts of fluids parenterally, such as dextrose solution, isotonic solution of three chlorides U. S. P., solutions of protein hydrolysates and often transfusions of whole blood or plasma.

Third, the treatment should be limited to those patients for whom accurate chemical data are available in regard to the status of the bicarbonate of the blood. The only exception would be its use in emergencies in which the clinical diagnosis of alkalosis is unquestioned.

Finally, because of its powerful acidifying action, until more is known about the tolerance of infants for ammonium chloride, the solution should be given subcutaneously whenever the patient's condition permits. If the need for intravenous administration arises, the injection should be made rather slowly.

CONCLUSIONS

In 9 infants with congenital hypertrophic pyloric stenosis, alkalosis of the metabolic type has been successfully ameliorated by the intravenous or subcutaneous injection of a solution of ammonium chloride in one-sixth molar concentration in isotonic solution of sodium chloride or isotonic solution of three chlorides U. S. P. (Ringer's solution).

It is suggested that this agent will be of value in the treatment of patients with extreme alkalosis and in the more rapid preparation of patients for operation.

Toxic effects were observed in only 1 patient, in whom the material was injected intravenously at an excessively rapid rate.

RELATIVE FREQUENCY OF "SUBCLINICAL" POLIOMYELITIS

Daily Temperature Studies on Intimate Contacts of Infectious Patients

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IN A coordinated study of poliomyelitis carried out in Chicago in the summer and fall of 1945 [1] daily temperature determinations were made on a number of the most intimate child contacts of patients with poliomyelitis. As a control similar studies were made on noncontacts living in the same block as the patient and on control children of the same age living ten and fifty blocks distant.[1a] By this procedure many fevers were detected in children who had no complaints of illness. As many of these as could be persuaded were checked several weeks later by examination of the spinal fluid. It is the purpose of this paper to report the incidence and clinical features of illnesses observed among these contact, noncontact and control children.

MATERIALS AND METHODS

After the entire project had been completed a detailed analysis of the work done by different investigators revealed that only those cases which had been investigated and reinvestigated were acceptable. It was also found that the physician investigators gave better and more detailed analyses of illnesses than the nurse investigators. Furthermore, in several cases in which nonparalytic poliomyelitis was reported by the clinical

From the laboratories of the Chicago Health Department and the Birmingham Baptist and Holy Name of Jesus Hospitals.

This work was supported in part by a grant from the Cook County Chapter of the National Foundation for Infantile Paralysis.

Most of the material in this paper was presented at a meeting of the Walker County, Alabama, Medical Society in November 1945.

1. (*a*) Casey, A. E.; Fishbein, W. I., and Bundesen, H. N.: Transmission of Poliomyelitis by Patient to Patient Contact, J. A. M. A. **129**:1141-1145 (Dec. 22) 1945. (*b*) Andelman, M. B.; Fishbein, W. I.; Casey, A. E., and Bundesen, H. N.: Spinal Fluid Protein in the Retrospective Diagnosis of Subclinical Poliomyelitis, Federation Proc. **5**:218, 1946; South. M. J. **39**:706-707 (Sept.) 1946.

staff the diagnosis was subsequently thought to be mumps associated with encephalitis. Consequently, material for this paper was limited to neighborhoods of paralytic patients with poliomyelitis and their control neighborhoods which had been investigated or reinvestigated (usually both) by one of us. This limited the data to nine neighborhoods in which daily temperatures were taken and specimens taken from nose, throat and stool up to twenty-one days after exposure among 22 intimate contacts of patients with poliomyelitis. None of these children gave a history of prior illness compatible with poliomyelitis during the entire summer or fall up to the time when the study was begun. A similar criterion was maintained for the 15 noncontacts from within a block of the paralytic patient and for the 37 control children from the nine control neighborhoods situated ten or fifty blocks distant from the patient's neighborhood. The observations were begun as soon as possible after the diagnosis of poliomyelitis had been made for the patient. However, there was a delay of five to seven days before studies were begun on those children who subsequently contracted what was believed to be poliomyelitis. Since virus specimens were collected during the incubation periods and during the first days of illness it should be possible to establish definitely in most instances (when the virus studies are completed) whether these minor illnesses were poliomyelitis. Furthermore, it is hoped the material will yield information on the distribution of the virus in nose, throat, mouth and stool during the late incubation period in the several types of poliomyelitis.

The procedure followed by the nurses in collecting the virus specimens was planned to avoid the carrying of virus from one child to another. The technic for the nose and throat swabs was that used for studies on diphtheria in the Chicago Health Department and was carried out by the nurses experienced in the diptheria technic. A certain amount of saliva was deliberately mixed with specimens of material from the throat. Stool specimens were collected by the mothers in ice cream cartons provided for the purpose. In taking the temperatures an individual thermometer in a special package was left in the home for each child studied. The same thermometer was used for axillary and rectal temperatures. The thermometer was placed under the child's arm for axillary temperature and left exactly five minutes. After this time it was shaken down, cleaned, rinsed, washed, lubricated and inserted in the rectum and kept exactly two minutes. It was read, removed with a sterile cotton pledget, wiped, cleansed with alcohol and soap without being touched by the nurses, returned to its special container and put away until the next day. Daily temperature determinations were made on the subjects in the study up to twenty-one days after known exposure to a patient with poliomyelitis (in its infectious period). Because the variation in rectal temperatures was great it was decided to use axillary

temperatures as the more dependable, especially since each had been read after the thermometer had remained in the axilla for five minutes.

In order to obtain standards and criteria for abnormal values, the daily temperature readings for 35 control children not used in this study were analyzed. These were from the seven control neighborhoods for nonparalytic patients investigated and reinvestigated by us and were entirely comparable and acceptable as controls. The axillary temperatures were distributed as follows:

96.0 F..... 1	97.4 F.....17	98.8 F.....11
96.2 2	97.6 27	99.0 4
96.4 0	97.8 19	99.2 6
96.6 2	98.0 37	99.4 2
96.8 3	98.2 49	99.6 0
97.0 26	98.4 36	99.8 1
97.2 13	98.6 36	100.0 1

There were 343 temperature determinations with a mean value of 98.10 F. Two of the children were ill during the course of the study, 1 with running nose and cold (4 CaSwi, wf 4½) whose temperatures were 99.2 F., 100 F., and 98.8 F., and the other with diarrhea and temperature of 99.8 F. and 98.8 F. (44 MaLig, cm 2½). If the twelve temperature readings for these 2 children are excluded, it will be seen that only two temperatures among the 331 were 99.4 F. or above. If the criterion of significant variation from the normal is 1 in 100 or less, then 99.4 F. may be taken as the beginning of significance. (The calculated 1 per cent point of the deviation is actually 99.48 F.)

Two other children (2 EdSch and 77 RoWas) had temperatures of 99.8 F., 98.4 F. and 99.2 F., and 98.8 F., 98.8 F. and 99 F. respectively. There were twenty temperatures of 98.8 F. and above among the 331 temperatures determined for the remaining 33 control children (an average of ten temperature readings for each child). It was unlikely, therefore, that the 2 children mentioned should have had five of the twenty temperatures 98.8 F. or above and even more unlikely that these temperatures should have occurred consecutively ($P=0.001$—) or on alternate days ($P=0.01$—).

Fevers were therefore defined for the study as (1) the presence of an axillary temperature of 98.8 F. or higher on two or more days, consecutively or alternately, or (2) the presence of an axillary temperature of 99.4 F. or higher on a single day. Delayed spinal fluid determinations were obtained for most of the children among the contacts who exhibited fever under observation, but it was almost impossible to obtain spinal fluid determinations for the noncontacts and the control children. The parents of the latter children were often enthusiastic about the survey but were rather reluctant to have spinal punctures made. In the particular series to be reported no spinal fluids were obtained from the noncontacts and the control children. Spinal fluid controls were obtained, however, as described elsewhere.[1b]

TABLE 1.—*Clinical Data on Twenty-Two Contact, Fifteen Noncontact and Thirty-Five Control Children Relating to Nine Chicago Neighborhoods with Paralytic Poliomyelitis* *

	Name	Race	Sex	Age, Yr.	Onset	Fever	Headache or Ache Along Spine	Stiff Neck or Back	Sore Throat	Constipation	Vomiting	Paralysis or Paresis	Running Nose	Cough	Diarrhea	Spinal Fluid: Cells	Spinal Fluid: Protein	Spinal Fluid: Date Puncture Made	Comment
TA	WiSha	W	M	7	8/ 5	+	+	+	+	+	0	+	0	0	0	36	44	8/ 7	
TA	LeLaF	W	M	1½	8/ 6	+	0	0	0	0	0	0	0	0	0	4	52	8/29	
TA	DoNei	W	M	10	8/ 9	+	0	0	0	+	0	0	0	0	0	3	76	9/14	
TA	ShGos	W	M	3½	8/17	+	+	0	+	0	+	0	0	0	0	10	blood	8/31	
TA	PaWeb	W	F	11	8/14	+	0	0	0	0	0	0	0	0	0	2	60	9/ 4	
TA	JoWeb	W	M	5½	8/15	+	0	0	0	0	0	0	0	0	0	10	70	9/ 4	
TA	GlDah	W	M	7	8/20	+	0	0	0	0	0	0	0	0	0	1	45	8/31	
TA	RoFye	W	F	2	8/20	+	?	+	+	0	?	0	0	0	0	45	68	8/20	
TA	MaTho	W	F	6	9/15	+	+	+	0	0	+	0	0	0	0	88	47	9/17	
TB	EaRap	W	M	11	7/23	+	0	0	0	0	0	0	0	0	0				
TB	PhOrz	W	M	6 mo.	8/10	+	0	0	0	0	0	0	0	0	0				
TB	WlEnr	W	M	3½	8/27	+	0	0	0	+	0	0	0	0	0	0	27	10/4	
TB	CaOls	W	F	10	8/27	+	0	0	0	+	0	0	0	0	0	2	39	10/8	
TB	CaKor	W	F	15 mo.	8/31	0	0	0	0	0	+	0	+	+	+	..	..	....	Cold
					9/ 8	+	0	0	0	0	0	0	0	0	0	..	..	....	Cutting molars
TD	JaRap	W	M	13	0	0	0	0	0	0	0	0	0	0	0				
TD	BoFah	W	M	3	0	0	0	0	0	0	0	0	0	0	0				
TD	MaFah	W	F	9	0	0	0	0	0	0	0	0	0	0	0				
TD	MaNei	W	F	17	0	0	0	0	0	0	0	0	0	0	0				
TD	RoSpe	W	M	11	0	0	0	0	0	0	0	0	0	0	0				
TD	BeWar	W	M	15	0	0	0	0	0	0	0	0	0	0	0				
TD	MaEBr	W	F	2½	0	0	0	0	0	0	0	0	0	0	0				
TD	RiJoh	W	M	6	0	0	0	0	0	0	0	0	0	0	0				
NC	PaRam	W	M	3	9/ 7	0	0	0	0	0	0	0	+	0	+				
NC	JeLoz	W	F	8	9/16	0	0	0	0	0	0	0	+	0	0	..	..	....	Cold
NC	JaHaw	W	M	2	9/14	0	0	0	0	+	0	0	0	0	0				
					10/16	0	0	0	+	0	0	0	+	+	0	..	..	....	Gland enlargement
ND	MaLWa	W	F	3	0	0	0	0	0	0	0	0	0	0	0				
ND	ArKlo	W	F	3½	0	0	0	0	0	0	0	0	0	0	0				
ND	HaRam	W	F	4	0	0	0	0	0	0	0	0	0	0	0				
ND	CaStr	W	F	3½	0	0	0	0	0	0	0	0	0	0	0				
ND	RoMOn	W	F	9½	0	0	0	0	0	0	0	0	0	0	0				
ND	RoFin	W	M	4	0	0	0	0	0	0	0	0	0	0	0				
ND	RuMSc	W	F	4½	0	0	0	0	0	0	0	0	0	0	0				
ND	CaRid	W	F	7½	0	0	0	0	0	0	0	0	0	0	0				
ND	WiFul	W	M	10	0	0	0	0	0	0	0	0	0	0	0				
ND	JiJur	W	F	4	0	0	0	0	0	0	0	0	0	0	0				

ND	KeHaw	W	M	4	0	0	0	0	0	0	0	0	0	0	0					
ND	MiFre	W	M	7½	0	0	0	0	0	0	0	0	0	0	0					
LB	CaAEr	W	F	3½	8/15	+	+	0	0	0	0	0	0	0	0					
					9/22	0	+	0	0	0	0	0	+	0	0					
LB	DoGed	W	M	4	9/ 1	+	0	0	+	0	0	0	0	0	0					
LB	DeBra	W	F	8	9/12	+	0	0	0	0	0	0	0	0	0					
LC	EdGre	W	F	7½	6/15	+	+	0	0	0	+	0	0	+	0	..	..	....		Pertussis
LC	PeGre	W	F	4	7/ 6	+	0	0	0	0	+	0	+	+	0	..	..	....		Pertussis
LC	JaRSo	W	M	4	8/11	0	0	0	0	0	0	0	+	0	0					
LC	JuCol	W	F	12	9/ 8	0	0	0	0	0	+	0	+	+	0	..	..	....		Pertussis
LC	WiCur	W	M	2½	0	0	0	0	0	0	0	0	0	0	0	..	..	....		Vaccinia
LC	RhSza	W	F	10	6/29	+	+	0	+	+	+	0	0	0	0	..	..	....		Mumps
LC	RoMar	W	M	1	8/ 5	+	0	0	0	0	0	0	+	0	0					
LC	NeHof	W	M	3	8/10	0	0	0	0	0	0	0	+	0	0					
LC	ShBen	W	F	4½	6/15	+	0	0	0	0	0	0	+	+	0	..	..	....		Measles
					6/22	+	+	0	+	0	0	0	0	0	0					
					9/16	0	0	0	0	0	0	0	+	0	0					
LC	WiBen	W	M	2	6/21	+	0	0	0	0	0	0	+	0	0	..	..	....		Measles
LC	JaWil	W	M	2	6/18	0	0	0	0	0	0	0	+	0	0					
					9/ 3	0	0	0	0	0	0	0	0	0	+					
					9/10	+	0	0	0	+	0	0	+	+	0					
					9/16	0	0	0	0	+	+	0	+	0	0					
LC	ThSte	W	M	9	8/20	+	0	0	+	0	0	0	0	+	0					
LC	KaSte	W	F	8 mo.	8/22	+	0	0	+	0	+	0	0	+	0	..	..	....		Teething
LC	FrCho	W	M	2	10/26	+	0	0	0	0	0	0	0	0	+					
LC	RoSum	W	M	4	10/26	+	+	0	+	+	0	0	+	+	0	..	..	....		Cold
LD	MaRus	W	M	1½	0	0	0	0	0	0	0	0	0	0	0					
LD	StSut	W	M	9	0	0	0	0	0	0	0	0	0	0	0					
LD	JaKit	W	F	9	0	0	0	0	0	0	0	0	0	0	0					
LD	DaQui	W	F	9	0	0	0	0	0	0	0	0	0	0	0					
LD	DiLar	W	F	6 mo.	0	0	0	0	0	0	0	0	0	0	0					
LD	CaLan	W	F	1½	0	0	0	0	0	0	0	0	0	0	0					
LD	JoLar	W	F	2½	0	0	0	0	0	0	0	0	0	0	0					
LD	RoLea	W	M	3	0	0	0	0	0	0	0	0	0	0	0					
LD	MaWil	W	F	4	0	0	0	0	0	0	0	0	0	0	0					
LD	KeNic	W	M	5	0	0	0	0	0	0	0	0	0	0	0					
LD	RoDav	W	M	10	0	0	0	0	0	0	0	0	0	0	0					
LD	HeBil	W	M	17	0	0	0	0	0	0	0	0	0	0	0					
LD	ElStu	W	F	2½	0	0	0	0	0	0	0	0	0	0	0					
LD	JoESk	W	F	27 mo.	0	0	0	0	0	0	0	0	0	0	0					
LD	KaHir	W	F	20 mo.	0	0	0	0	0	0	0	0	0	0	0	..	..	....		Measles
LD	LeCSk	W	M	5	0	0	0	0	0	0	0	0	0	0	0					
LD	JuKin	W	F	2	0	0	0	0	0	0	0	0	0	0	0					
LD	CaOMa	W	F	5	0	0	0	0	0	0	0	0	0	0	0					
LD	RiCra	W	F	4	0	0	0	0	0	0	0	0	0	0	0					

* Interpretation of the letters in the first column is as follows: T, contacts; N, noncontacts; L, controls; A, children having fever and other symptoms compatible with a clinical diagnosis of poliomyelitis; B, children having minor illnesses compatible with but not diagnostic of poliomyelitis; C, children having minor illnesses not suggestive of poliomyelitis; D, children without evidence or history of illness during the summer and early fall.

TABLE 2.—*Fevers Among Contacts, Noncontacts and Controls Detected by Daily Determination of Axillary Temperatures* *

		Name	Race	Sex	Age, Yr.	DI	DS	Date	Fever	Date	Fever	Date	Fever	Type	Spinal Fluid Cells	PA	PR	Date	Comment
5	TA	WiSha	W	M	7	9	5	8/ 6	100.0	and on other dates				ParP	36	+	44	8/ 7	
18	TA	RoFye	W	F	2	15	5	8/20	101.4	and on other dates				MenP	45	+	68	8/21	
48	TA	MaTho	W	F	6	25	19	9/15	100.8	(6 days after end of study)				MenP	88	0	47	9/17	
11	TA	ShGos	W	M	3½	12	3	8/17	99.4	8/18	100.0	....	....	AboP	10	+	blood	8/31	
5	TA	DoNei	W	M	10	8	1	8/ 3	98.8	8/ 9	99.0	8/11	99.0	AboP	3	+	76	9/14	
48	TB	WiEnr	W	M	3½	8	1	8/27 8/31	99.4 99.0	8/28 9/ 1	99.2 99.2	8/29 9/ 2	99.0 99.0	AboP	0	0	27	10/ 4	
48	TB	CaOls	W	F	10	8	1	8/27	98.8	8/28	99.2	8/31	98.8	AboP	2	+	39	10/ 8	
82	TB	CaKor	W	F	15 mo.	18	7	9/ 8 9/11	99.2 99.0	9/ 9 9/12	99.4 99.0	9/10	98.8	?					
38	TA	GlDah	W	M	7	15	5	8/20 9/10	.... 99.0	8/31	99.8	9/ 2	99.4	AsyP	1	0	45	9/ 1	
5	TA	LeLaF	W	M	1½	10	5	8/ 6	99.4	....	....	....	....	AsyP	4	0	52	8/29	
1	TB	EaRap	W	M	11	15	2	7/23	99.0	7/25	99.0	....	....	?					
11	TA	JoWeb	W	M	5½	12	1	8/15	99.0	8/16	99.0	....	....	AsyP	10	4+	blood	9/ 4	
11	TA	PaWeb	W	F	11	12	1	8/14	99.0	8/27	99.0	....	....	AsyP	2	0	60	9/ 4	
5	TB	PhOrz	W	M	6 mo.	7	9	8/10	98.8	8/16	99.8	....	....	?					
5	LC	WiCur	W	M	2	..	12	8/13	98.8	8/14	98.8	....	....	.....	..	..	..	....	Vaccinia
10	LB	CaAEr	W	F	3½	..	4	8/15	98.8	8/15	99.0	8/16	99.6						
10	LB	DoGed	W	M	4	..	21	9/ 1	?	(5 days after end of study)									
101	LB	DeBra	W	F	8	..	6	9/12	99.4	9/14	99.2	9/20	99.2						
203	LC	FrCho	W	M	2	..	7	10/26	100.0	....	....	....	....	.....	..	..	..	....	Diarrhea
203	LC	RoSum	W	M	4	..	7	10/26 10/29	100.0 99.8	10/27 10/30	100.4 99.4	10/28	100.0	.....	..	..	..	....	Running nose, cough

* The letters in the first column are interpreted in table 1. Interpretations of other abbreviations in this table are as follows: DI, days between contact and onset of fever; DS, days from start of field study to onset of fever; PA, Pandy; PR, protein; ParP, paralytic poliomyelitis; MenP, meningismic poliomyelitis; AboP, subclinical myelitis with symptoms; AsyP, subclinical poliomyelitis without recorded symptoms.

As in other studies,[2] the infectious period was defined as three days before or three days after the onset of the prodromal period, and the incubation period as five to thirty-five days, but usually seven to twenty-one days. Intimate contacts were children (under 25 years) who spent more than ten minutes in play or had other close contact with a patient or suspected patient in the infectious period.

RESULTS

Among the 22 children who had been in contact with a patient with poliomyelitis in its infectious period 14 showed a fever compatible with poliomyelitis between seven and twenty-five days after exposure. None of the 15 noncontacts living within the same block as the patient had a fever compatible with poliomyelitis. Three of the 37 control children living ten or fifty blocks distant from the patient with poliomyelitis had fevers compatible with but not diagnostic of poliomyelitis, and 3 others had fevers considered incompatible with poliomyelitis (vaccinia, coryza and diarrhea; table 2). Therefore, among the 52 noncontacts and control children there were 3 febrile illnesses compatible with but not diagnostic of poliomyelitis, this being the percentage (6 per cent) previously reported in such neighborhoods.[1a] In contrast to this there were 14 fevers among the 22 contacts (64 per cent), and 9 were definitely diagnosed as poliomyelitis. This difference between the two groups is statistically significant ($\chi^2 = 28.8$; $N = 1$; $P = 0.0001$—). When the children over 12 years of age were eliminated from contacts, noncontacts and controls, there were 14 fevers among 19 children in the contact group (74 per cent) as compared with 3 fevers compatible with poliomyelitis among 47 children in the noncontact and control groups under 12 years of age (6 per cent). (The 3 children with fevers considered incompatible with poliomyelitis were eliminated from this computation.) This indicates a high degree of communicability for poliomyelitis during its infectious period for children under 12 years of age. These results, in a more carefully selected group, completely confirm the neighborhood studies in which reliance on careful histories was the principal working tool.[1a]

The average period of incubation for the 14 fevers as estimated from the period of greatest exposure was twelve and four-tenths days, which is compatible with results previously reported.[3] There seems to be no

2. (*a*) Casey, Fishbein and Bundesen.[1a] (*b*) Andelman, Fishbein, Casey and Bundesen.[1b] (*c*) Casey, A. E.: Observations on an Epidemic of Poliomyelitis, Science **95**:359-396 (April) 1942; (*d*) Incubation Period in Epidemic Poliomyelitis, J. A. M. A. **120**:805-807 (Nov. 14) 1942. (*e*) Aycock, W. L., and Kessel, J. F.: Infectious Period of Poliomyelitis and Virus Detection, Am. J. M. Sc. **205**:454-465 (March) 1943.

3. Casey, Fishbein and Bundesen.[1a] Casey.[2c,d] Aycock and Kessel.[2e]

difference in the incubation period among the cases of mild and severe disease, as was surmised in an earlier study.[2c]

The clinical features of the 14 illnesses thought compatible with poliomyelitis are summarized as follows: only 1 developed into paralytic poliomyelitis (7.2 per cent); 2 others were diagnosed as "meningismic" poliomyelitis with stiff neck, stiff back, head drop and other spinal fluid features of nonparalytic poliomyelitis (14 per cent). Four other children (28.6 per cent) had mild symptoms including constipation, vomiting, sore throat or headache in addition to the fever, and an absence of running nose, cough or diarrhea (TADoNei, TAShGos, TBWiEnr and TBCaOls). Paralysis, stiff neck and stiff back were also absent, and the pediatricians in the study failed to confirm the cases as poliomyelitis. Delayed examinations of the spinal fluid [1b] were performed on the 4 children; the cells were increased in 1 and the spinal fluid protein level elevated in another. Unfortunately, examinations of the spinal fluid of the 2 other children were made thirty-nine to forty-three days after the onset of the fever. In another paper of this series [1b] it has been shown that the spinal fluid protein is usually returning to normal by this time. The 7 remaining children (50 per cent) with temperatures varying from 98.8 F. to 99.8 F. on successive days had no clinical symptoms (table 2). No symptoms or physical signs of illness were obtained by the visiting nurses, visiting pediatricians or members of the family. Determinations of spinal fluid protein were made for 4 of the 7 and revealed levels of 45, 52, 60 and 70 mg. respectively on the eleventh, twenty-fifth, twenty-first and twentieth day respectively after the onset of the fever (table 2).

COMMENT

It should be kept in mind that this is only a preliminary series, but it is believed to have some value because of the rigid selection of material. Between July 1 and Nov. 15, 1945, 233 cases of poliomyelitis were reported in the city of Chicago. Personnel in the research group were able to make preliminary investigations in the neighborhoods of 74 patients, 41 of these being paralytic. It was not possible for the authors to investigate and reinvestigate other than the nine control and patient neighborhoods of the 11 paralytic patients reported on in this study, and the seven control and patient neighborhoods of 7 nonparalytic patients. Of the latter material only the control data are used in the study (in the section on materials and methods).

The determination of daily temperatures of patient contacts was the second of four epidemiologic tools in the field studies of 1945. The first (described and utilized in the first article of this series) [1a] was reliance on careful histories and neighborhood studies; the third epidemiologic tool was the examinations of spinal fluid two to five weeks after the onset of fever,[1b] and the fourth was, of course, the determination of the

presence of the virus in specimens taken from the nose, throat, mouth and stools of those persons whose temperatures were taken. Because of a shortage of animals virus studies are not yet completed. All of the material in the present study had the benefit, however, of the best investigations and reinvestigations. A number of those who experienced febrile illnesses had spinal puncture performed and all have virus specimens available for inoculation.[4]

Among the 41 paralytic cases of poliomyelitis studied in Chicago during 1945 there were 4 deaths (10 per cent), and in 67 per cent there was clinical recovery. Therefore, if these percentages are applied to the small series of 14 cases at hand, it is roughly [5] estimated that the case fatality from poliomyelitis was 0.7 per cent, that 2 per cent were paralytic cases with permanent residue, that 5 per cent were paralytic cases with clinical recovery, that 14 per cent were nonparalytic cases of the meningismic type (i. e. with stiff neck, stiff back, head drop, etc.)

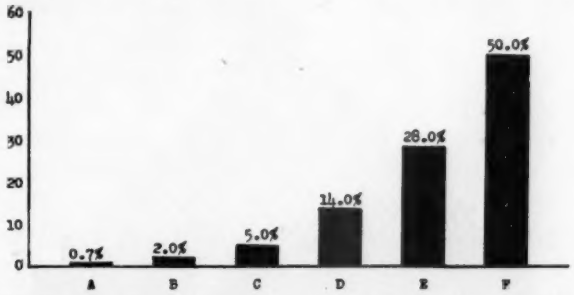

Fig. 1.—Estimated analysis of 100 consecutive cases of poliomyelitis. *A*, fatal cases. *B*, cases involving permanent paralysis. *C*, cases involving paralysis with recovery. *D*, cases of "meningismic" poliomyelitis. *E*, cases of subclinical poliomyelitis with mild symptoms. *F*, cases of subclinical poliomyelitis without recorded symptoms.

and clinical recovery, that 28 per cent were nonmeningismic and nonparalytic cases with symptoms compatible with poliomyelitis (headache, vomiting, fever, elevated spinal fluid protein, etc.) and that 50 per cent were cases of poliomyelitis with mild fevers but no other recorded symptoms or signs except an elevation of the spinal fluid protein above 45 mg. two to five weeks after onset (figs. 1 and 2).

The extreme mildness of poliomyelitis, if present studies are correct, is a cause for regret that the wealth of research on the disease has been concentrated on the 2 per cent of children who are most severely affected and that almost no systematic study is available on the usual

4. Since this paper was presented for publication inoculation of stools has revealed the presence of virus just before or at the onset of the prodrome among most of those contact children with subclinical fevers.[6]

5. This entire study is being repeated in Chicago in 1946 to obtain more data on all points.

clinical manifestations of the disease (98 per cent). The Chicago studies in 1945 were not planned to establish the presence or absence of an extrahuman reservoir of the virus during interepidemic periods or to establish whether the nonparalytic disease is prevalent during the winter months in northern climates in sufficient degree to carry the virus over to the ensuing summer.

The failure to elicit other symptoms or signs in 50 per cent of the children in the present series with fever and subsequent elevation of the spinal fluid protein does not indicate that these were not present. These mild fevers were analyzed only near the termination of the study, and we did not always have the opportunity of checking the children during the so-called asymptomatic febrile period for mild symptoms or signs. The pediatricians, visiting nurses and parents who saw the children during this phase may have been looking for more serious complaints and thus may have overlooked minor complaints,

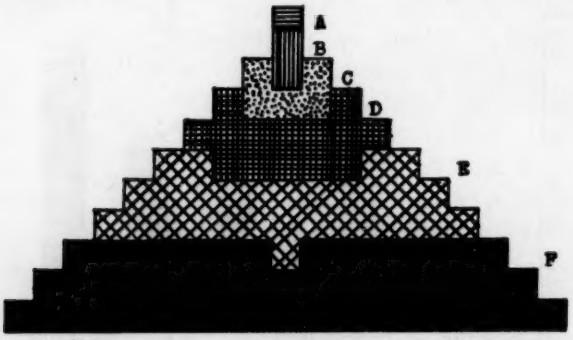

Fig. 2.—Estimated analysis of 100 consecutive cases of poliomyelitis. An interpretation of the letters is given in the legend for figure 1.

such as headache, sore throat, vomiting and constipation, although they had been asked to record them.

It will be recalled that fevers were detected by daily axillary temperatures in 14 (74 per cent) of 19 children under 12 years of age in the contact groups within five to twenty-one days after exposure. Two of the 5 who did not show fever probably had been exposed more than seven days before the study began. In a stool of 1 of these (TDMaEBr, wf 2½) virus was detected.[6] For children known to have been in intimate contact for more than ten minutes with a patient with infantile paralysis in its infectious period, examined closely up to twenty-one days after exposure, the following apparent incidence of poliomyelitis was detected.

Ages	Interval	Number	Percentage
½ - 3 yr.	2½ yr.	5 out of 5	100
3 - 8 yr.	5 yr.	6 out of 8	75
8 - 18 yr.	10 yr.	4 out of 9	44

6. Gordon, F. B., and others: Unpublished material.

If these data can be substantiated by currently planned studies in 1946, one must conclude that poliomyelitis is the most communicable disease known, even more so than measles and chickenpox.

As to the clinical features, it should be pointed out (table 1) that not a single child in this group had running nose, cough or diarrhea. Studies [1a] of the histories indicated that the chances were about 1 in 20 that a fever with any of these symptoms was poliomyelitis, and about 1 in 100 that a fever with a combination of these was poliomyelitis. We wish to stress, therefore, the negative value of the symptoms running nose, cough and diarrhea in the differential diagnosis of subclinical poliomyelitis. If to these is added carefully taken daily temperatures on intimate child contacts during the infectious period and determinations of spinal fluid protein twenty-one to thirty days after the onset of the fever, it is believed the pediatrician will have all that is needed for the recognition of subclinical poliomyelitis until some simple serologic or other test is available or unless the family is wealthy enough to pay for inoculation of animals with pooled stools collected during the incubation and prodromal periods in the suspected case of mild disease.

Wickman,[7] Frost,[8] Draper,[9] Aycock and Luther,[10] Paul, Salinger and Trask [11] and many others have reported that poliomyelitis without stiff neck, paralysis or paresis is common. However, no standardized criteria or epidemiologic tools were used by which the subclinical disease could be adequately recognized. It was also generally implied that the milder forms of the disease affected the nose, throat or gastrointestinal tract but failed to produce lesions of the central nervous system or elevated levels of spinal fluid protein [11] and were, therefore, "abortive." Since the work was not based on careful histories of definite exposure to poliomyelitis in its infectious period, daily temperatures were not determined on the exposed population, and spinal fluid determinations of a delayed nature were not performed in the cases of mild disease,

7. Wickman, I.: Acute Poliomyelitis, translated by J. W. Maloney, Nervous and Mental Disease Monograph 16, New York, Nervous and Mental Disease Publishing Company, 1913.

8. Frost, W. H.: Epidemiologic Studies of Acute Anterior Poliomyelitis, Hygienic Laboratory Bulletin 90, United States Treasury Department, 1913, p. 29.

9. Draper, G.: Acute Anterior Poliomyelitis, in Nelson Loose-Leaf Living Medicine, New York, Thos. Nelson & Sons, 1926, vol. 2, p. 67.

10. Aycock, W. L., and Luther, E. H.: The Incubation Period of Poliomyelitis, J. Prev. Med. **3**:103-120 (March) 1929.

11. Paul, J.; Salinger, R., and Trask, J. D.: Studies on the Epidemiology of Poliomyelitis: Methods and Criteria for the Detection of Abortive Poliomyelitis, Am. J. Hyg. **17**:587-600 (May) 1933. Paul, J. R.; Salinger, R., and Trask, J. D.: Studies on Epidemiology of Poliomyelitis: Incidence of Abortive Types of Poliomyelitis, ibid. **17**:601-612 (May) 1933.

previous estimates of the incidence of poliomyelitis must be classed as largely guesswork. Our studies, on the other hand, have shown that clearly definable criteria for subclinical poliomyelitis are probably always available and that the disease may always involve the central nervous system; also that, despite minimal clinical manifestations, the disease produces a profound systemic effect suggestive of an immunizing process (delayed rise in spinal fluid protein).[1a]

We believe, therefore, that our studies are unique for the following reasons: 1. Unusually carefully taken histories recorded the events that transpired in exposed population and in two other populations not so exposed (noncontacts and controls). 2. Children giving a history during the preceding two months of fever which seemed at all compatible with poliomyelitis were eliminated (together with their contacts) from the numbers of persons presumed susceptible to the disease. 3. Daily determinations of axillary temperatures were made for the children in the three populations, namely, those exposed and the two groups presumably not exposed. 4. The virus specimens from the nose, throat and stool were collected systematically during the incubation and prodromal periods and at variable times afterward; thus an entirely unique body of data was given for virus and epidemiologic studies. 5. Since it was found that the spinal fluid protein was elevated between two and five weeks after onset in subclinical cases, as many patients as could be persuaded were subjected to spinal puncture. 6. Since the temperature study was coordinated with the three other epidemiologic tools a more complete picture of poliomyelitis in a neighborhood was probably obtained than has been obtained heretofore.

Attempts by other authors to study the epidemiology of poliomyelitis have revealed a low incidence of patient to patient contact, usually 20 to 30 per cent, according to Maxcy.[12] The present material offers a probable explanation. Such studies have accepted as cases of poliomyelitis only the ones in which there is paralysis, paresis, stiff neck or stiff back, amounting to about 22 per cent of the total cases of poliomyelitis if the present study is correct. Therefore, only 22 per cent of patients with poliomyelitis investigated would have been expected to have had contact with a patient having paralysis (paralytic) or having a stiff neck or stiff back (meningismic type).

SUMMARY

Daily determinations of the axillary temperature were made between five and twenty-five days (in most instances six and twenty-one days) after the known exposure of 22 children to a patient with poliomyelitis

12. Maxcy, K. F.: A Review of the Epidemiology of Acute Anterior Poliomyelitis with Reference to the Mode of Transmission, Journal-Lancet **64**:216-223 (July) 1944.

in the infectious period. Among 22 children studied who had had such intimate contacts 14 had a febrile illness between seven and twenty-five days after exposure. This illness was believed to have been poliomyelitis. No such febrile illness was detected among 15 noncontacts who lived within a radius of one block of the patients and were of comparable age with the contacts. Three of 37 control children living in neighborhoods ten or fifty blocks distant from the patient experienced febrile illnesses considered compatible with poliomyelitis, but none was diagnosed as such.

Among the 14 contacts who had fever considered compatible with poliomyelitis, 1 had frank poliomyelitis with transient paralysis and 2 had frank poliomyelitis without paralysis but with stiff neck, stiff back, head drop and increased cells and elevated protein in the spinal fluid. Four other children (28 per cent) had fevers and mild symptoms but were without stiff neck, stiff back or paralysis. Two of these were checked by examination of the spinal fluid between two and five weeks after the onset of the fever, and the spinal fluid protein was elevated above 45 mg. in each instance. The other 7 children (50 per cent) had axillary temperatures ranging from 98.8 F. to 99.8 F. and seemed to have no symptoms. Four of the 7 were checked by examination of the spinal fluid two to four weeks later, and each child had a spinal fluid protein level of 45 mg. or above.

All of the 5 contact children who were 6 months to 3 years of age had illnesses compatible with poliomyelitis within six to twenty-one days after exposure (100 per cent); 6 of 8 contact children 3 to 8 years of age (75 per cent) had illnesses compatible with poliomyelitis within six to twenty-one days after exposure; 4 of the 9 children 8 to 18 years of age (44 per cent) had illnesses compatible with poliomyelitis within six to twenty-one days after exposure.

The evidence, although scant and needing the benefit of continued investigation, is sufficient to indicate that perhaps 98 per cent of poliomyelitis is a mild, widespread, highly communicable disease of young children leaving no residual paralysis. Transient paralysis occurs in about 5 per cent of all cases and the meningitic form (nonparalytic but with stiff neck or stiff back, head drop and increased cells and protein in the spinal fluid in the first week) in about 14 per cent. The fatality rate seems not to exceed 0.7 per cent. Residual paralysis in poliomyelitis seems an infrequent complication, and perhaps not more than 1 child in 40 or 50 is so affected.

The following simple clinical procedures seem available in general practice: (1) the isolation of the most intimate child contacts of an infectious patient during the period five to fifteen days after exposure; (2) daily determinations of axillary temperature for the child during this

period of isolation, and (3) if temperatures of 99.4 F. on a single day or 98.8 F. or more on consecutive or alternate days are detected, the collection of the first 3 stools. The chances that in a suspected case the patient has poliomyelitis seem about 1 in 12 if diarrhea is present and about 1 in 20 or 25 if either running nose or cough is present; the chances that the condition is poliomyelitis with a combination of any two of these symptoms are remote. Determination of spinal fluid protein three to five weeks after the onset of fever is recommended in suspected cases. A high temperature without stiff neck, stiff back or head drop seems rare in subclinical poliomyelitis.

ANOMALOUS ORIGIN OF THE LEFT CORONARY ARTERY

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AMONG the various anomalies of the coronary arteries, the type in which the left coronary artery arises from the pulmonary artery produces characteristic effects which may permit diagnosis during the lifetime of the patient. The 2 cases of this kind which are reported here are of interest because the relatively long period of observation made it possible to follow in detail the clinical course and the complications. Emphasis will be placed on some of the symptoms which have been mentioned before and on several pathologic changes which have not been reported previously.

REPORT OF CASES

CASE 1.—*Summary.*—This patient had persistent symptoms of respiratory disease from the first week of life until the time of her death at the age of 6 months. The heart was greatly enlarged, and in the electrocardiogram the T waves in lead I were inverted. At autopsy a narrow left coronary artery was found to have its origin in the pulmonary artery. There were extensive endocardial fibrosis, myocardial degeneration and fibrosis just beneath the endocardium, an infarct in the left ventricle and acute epicarditis.

Details.—The infant was a Negro girl born Jan. 17, 1945, following a normal labor and delivery. The mother had syphilis and had received treatment for the infection only during the last two months of pregnancy. The serologic reaction of the father's blood was not known, but he was in good health, and there was no history of cardiac disease or other congenital anomalies in either branch of the family. There were no other children.

The infant weighed 7 pounds and 7 ounces (3,374 Gm.) and seemed normal at birth, but began to cough a few days later. At the age of 6 weeks the cough was severe and vomiting occurred frequently. The patient often gagged when she attempted to take her milk, and a large amount of phlegm flowed from the mouth, at which times her color became slightly cyanotic.

On March 10, when the infant was approximately 8 weeks old, she was admitted to the hospital. The most striking symptom at this time was the respiratory distress. The rate of breathing was rapid, and there seemed to be some impediment of the expiratory phase of respiration. The percussion note was dull in the right upper portion of the chest, and rales could be heard in this location. Consolidation in this area was demonstrated by roentgenograms. A tentative diagnosis of pneu-

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monia was made, but the infant's symptoms were in no way relieved by the administration of sulfadiazine for a period of approximately one week.

Laboratory examinations failed to reveal any other abnormal condition. The Kahn test was negative. The tuberculin test was negative. The hemoglobin values varied from 9.9 Gm. to 12.2 Gm. and the number of red cells from 3,200,000 to 4,050,000 per cubic millimeter. The number of white cells on several different occasions was approximately 10,000 per cubic millimeter, with normal differential counts. The urine was negative except for traces of albumin.

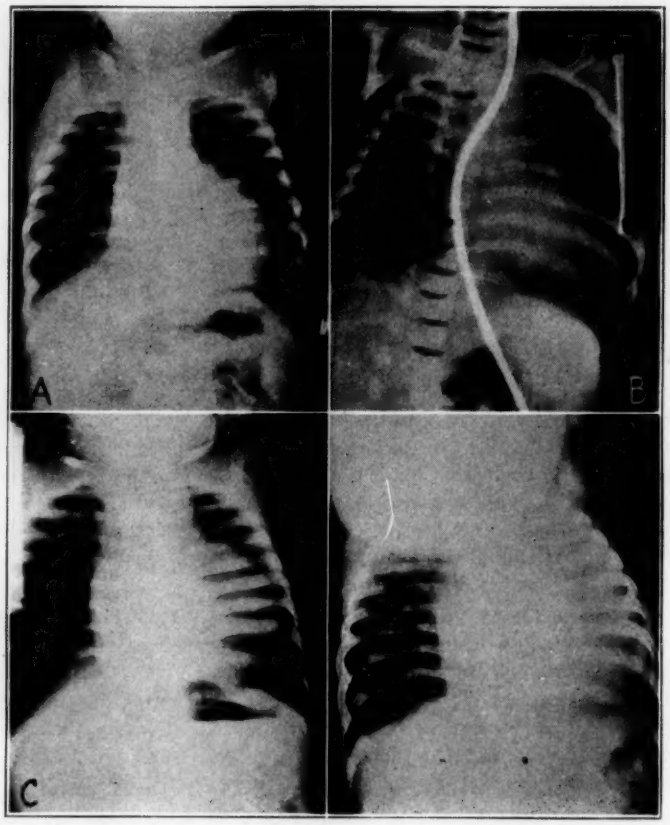

Fig. 1.—Teleoroentgenograms of patient 1. *A*, taken April 16, 1945, when patient was 3 months old; enlarged heart and opacity at the right upper lung field may be seen. *B*, right oblique view taken April 24 with a barium-filled catheter in the esophagus; esophagus is displaced posteriorly by the heart. *C*, taken June 4, when the patient was 4½ months old; a larger heart and opacities at both upper lung fields may be seen. *D*, taken July 14, when the patient was 6 months old; clouding of the entire left lung field may be seen.

During a ten week period the area of haziness at the upper lobe of the right lung gradually diminished in size and density in the roentgenograms (fig. 1), but the patient's respiratory distress continued. She was kept in an oxygen tent for one month but seemed no better in the tent than out. Bronchoscopic examination failed to reveal any obstruction of the larger air passages.

Throughout the stay in the hospital, food was taken with difficulty because of the respiratory distress but vomiting occurred only occasionally and there were no severe attacks of cyanosis or symptoms suggesting pain. She gained weight slowly, about 2½ pounds (1,134 Gm.) in three months. She weighed 13 pounds, 2 ounces (5,953 Gm.) at the end of this period.

Approximately one month after admission of the patient to the hospital, the roentgenograms first demonstrated an increase in the size of the heart. The cardiac width in the ventricular area at this time was 7.2 cm., and the internal diameter of the chest was 12 cm. Attention was then directed toward the heart, and lateral roentgenograms with iodized poppyseed oil (40 per cent) in the esophagus showed enlargement of the heart posteriorly (fig. 1). In the electrocardiogram, a definite inversion of the T wave in lead I suggested the possibility of a defect of the coronary arteries (fig. 2).

The patient improved somewhat and was discharged from the hospital at about 5 months of age. Five weeks after discharge, when she was approximately 6 months old, the patient was seen in the dispensary. During the preceding week,

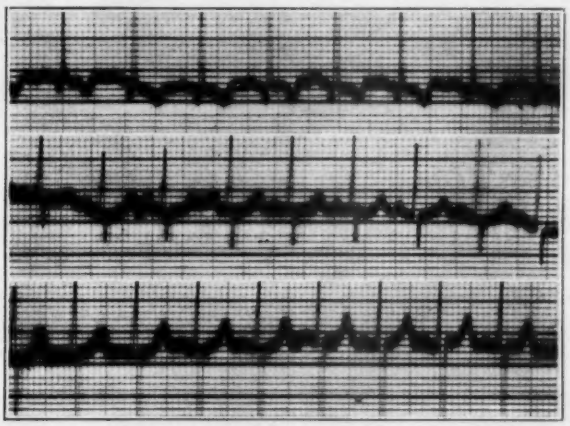

Fig. 2.—Electrocardiogram of patient 1 taken May 14, 1945, showing inversion of T waves in lead I.

she had had fever and pronounced respiratory distress. She weighed only 12 pounds, 10 ounces (5,727 Gm.) at this time. She was readmitted to the hospital at once.

The physical findings were now predominantly on the left side of the chest. The heart was greatly enlarged, but there were no murmurs, and the sounds were generally of good quality. The percussion note over the entire left side of the chest was flat, the breath sounds were diminished in intensity, and occasional rales could be heard throughout this area. In the roentgenograms the entire lung field on the left was cloudy and there was a suggestion of accumulation of fluid in the lower portion of that side of the chest. The liver was slightly enlarged. The hemoglobin value was 11.4 Gm., the number of red cells 3,700,000 per cubic millimeter and the number of white cells 10,950, with a normal distribution of the various forms of white cells. The urine contained traces of albumin and acetone. The content of carbon dioxide in the plasma was 28.3 volumes and that of chlorides was 99.6 milliequivalents per liter; the blood sugar level was 92 mg. per hundred cubic centimeters.

To offer some relief to the patient, thoracentesis was performed by insertion of a needle in the fifth interspace in the axillary line. Twenty cubic centimeters of a cloudy fluid was removed which, on culture, proved to be sterile.

The patient died July 17, at the age of 6 months.

Necrospy: Gross examination. Necropsy was limited to the examination of heart and lungs. The thorax was symmetric, and approximately 20 cc. of clear fluid was present in each pleural cavity. The thymus was of average size. The pericardial sac was huge and almost filled the entire left side of the thorax. It extended 6.3 cm. to the left of the midline and almost touched the left lateral wall of the chest. It compressed the left lung against the posterior and mediastinal portion of the left side of the thorax. Its greatest transverse measurement was 9 cm., while the greatest width of the thorax was 12.7 cm. The right lung was quite voluminous, and the anterior border overlapped the right border of the pericardial sac anteriorly. Approximately 10 cc. of amber fluid, containing strands of

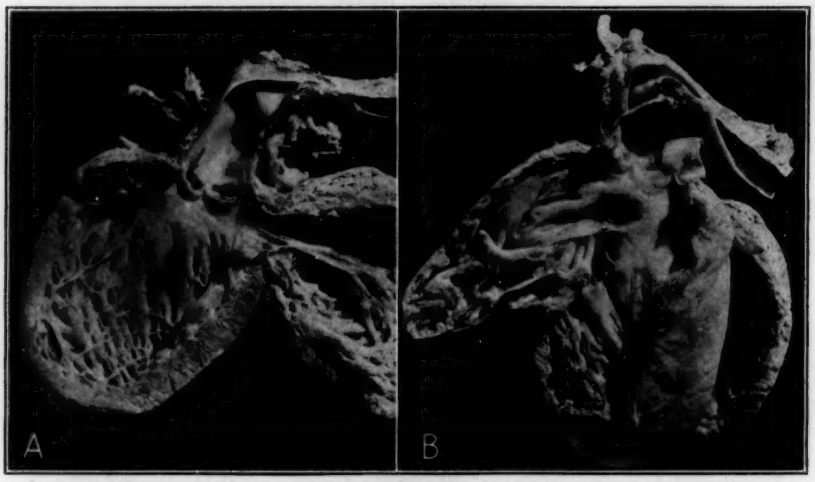

Fig. 3 (case 1).—*A*, hypertrophy and dilatation of the left ventricle; ostium of the right coronary artery may be seen behind the right cusp of the aortic valve. *B*, right ventricle; ostium of the left coronary artery may be seen behind the left posterior cusp of the pulmonary valve.

light tan fibrin, were present in the sac, and a thin fibrinous exudate was spread over the serous surface of the sac. The visceral and parietal layers were adherent over the lateral aspect of the left ventricle.

The heart was large and globular (fig. 3). It weighed 120 Gm., which is approximately three times normal weight. The great veins and arteries entered and emerged from the heart normally. There were no abnormalities of the cardiac valves or defects of the septums. The ductus arteriosus was obliterated. The right atrium and the right ventricle were not dilated, and the right ventricular wall, which measured 4 mm. in thickness, was only slightly hypertrophied. The left atrium was smaller than normal and was lined by a slightly thickened gray opaque endocardium. The left ventricular wall was obviously hypertrophied and varied in thickness from 5 mm. at the apex to 10 mm. along the lateral wall. There was enormous dilatation of the ventricle and a slight bulging of the interventricular

septum into the right ventricle. The left papillary muscles and the columnae carneae were markedly flattened, and the entire endocardium was thick, gray and opaque.

The right coronary artery, which arose behind the right aortic cusp, was of average size and lined by a smooth gray intima. It coursed along the posterior atrioventricular groove and the posterior interventricular septum. The left coronary artery arose behind the left posterior cusp of the pulmonary valve, curved around the

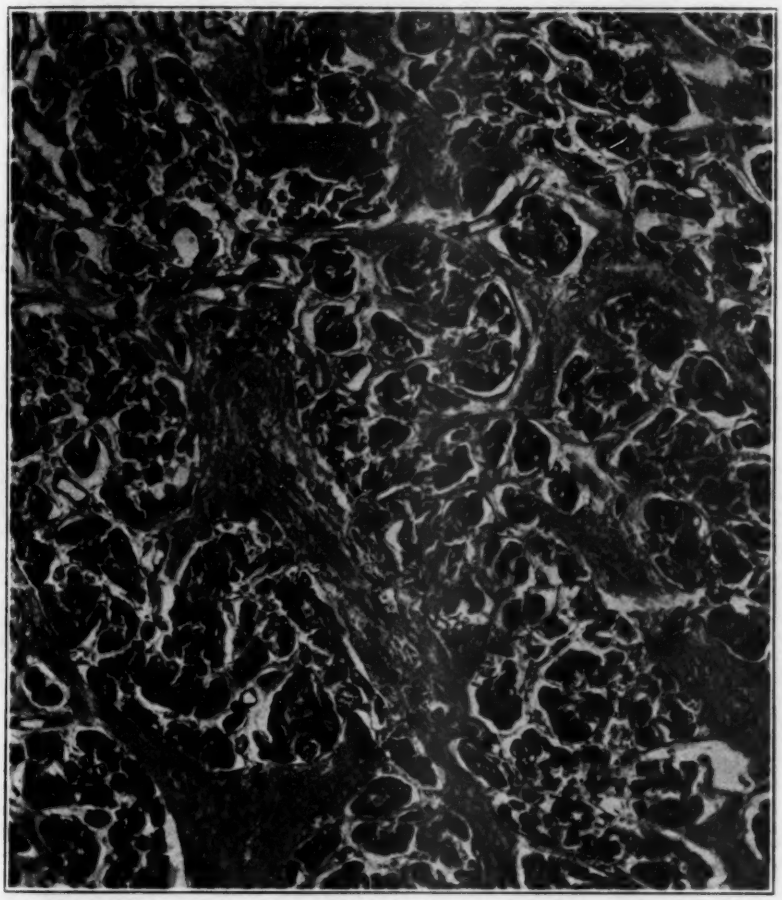

Fig. 4 (case 1).—Narrow and wide bands of fibrous tissue replacing bundles of muscle cells.

pulmonary artery and immediately branched into a narrow anterior descending branch and a narrow thin-walled circumflex branch. The ostium of the artery was small but patent and the intima was smooth and gray. The pulmonary artery and the aorta appeared normal, and there was no coarctation of the latter.

The myocardium was generally light red and firm, but it was darkly reddened in one large area, 3 cm. in diameter, situated on the lateral aspect of the left ventricular wall in the region supplied by the left circumflex artery. The overlying

epicardial surface was also darkly reddened and covered by a considerably thicker fibrinous exudate.

The right lung was voluminous, emphysematous and pink, although a few small dark reddish blue areas of atelectasis were present in the upper and lower lobes. The left lung, except for an emphysematous lingual tip, was small, collapsed, dark blue and practically airless. The bronchi were normal.

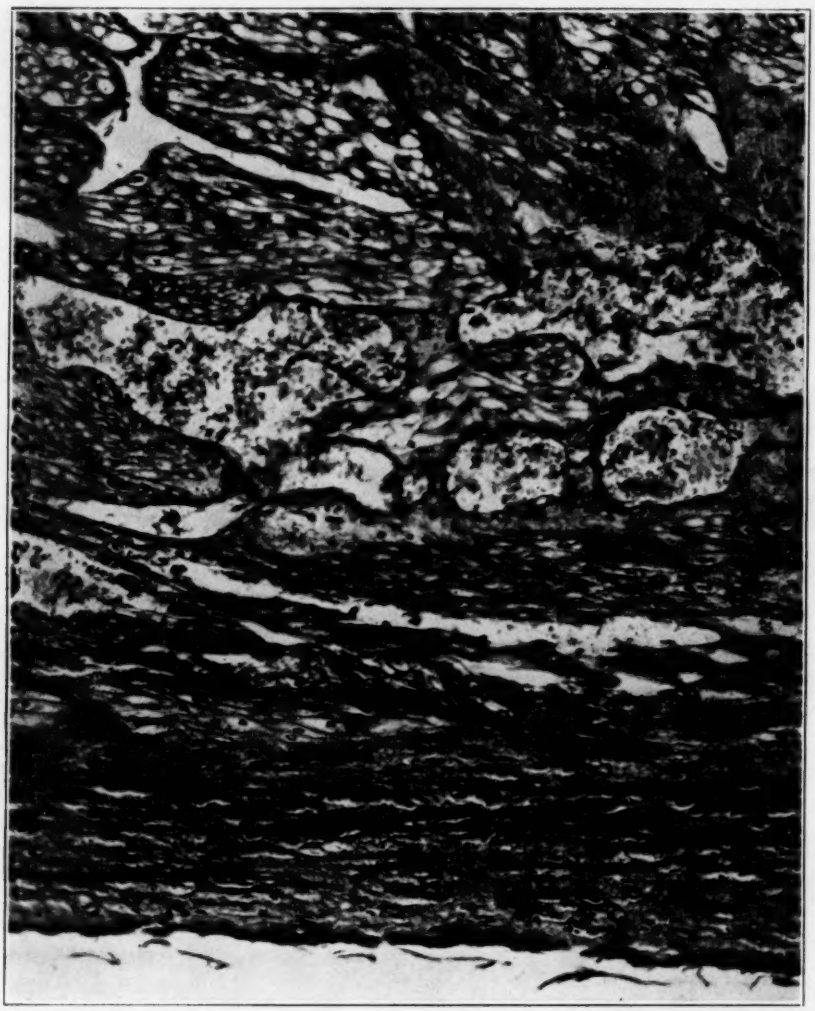

Fig. 5 (case 1).—Left ventricle; fibrosis of the endocardium; extensive degeneration of subjacent muscle cells; dilated blood-filled embryonic sinusoids.

Microscopic examination. Moderate congestion, slight edema and varying degree of proliferation of connective tissue and infiltration of polymorphonuclear leukocytes occurred in the epicardium. Cloudy swelling with fading of the striations was evident in the subjacent myocardium and was most pronounced in an area

of the lateral portion of the left ventricle where there was an added polymorphonuclear leukocytic reaction. The capillaries throughout the entire myocardium were engorged, and the interstitial tissue was edematous. Thin and moderately thick bands of dense connective tissue formed streaks through the myocardium and appeared to radiate from some small arteries and veins (fig. 4). A few of the arteries had narrowed lumens due to intimal proliferative changes. The greatest morphologic alterations were observed in the endocardium and immediately subjacent myocardium. The endocardium was greatly thickened by fibroelastic tissue which surrounded and followed the thebesian veins into the myocardium. The cytoplasm of the subendocardial muscle cells was vacuolated, and many of the cells were isolated by bands of connective tissue and were undergoing atrophy and replacement by scar tissue. Superimposed on such a picture but not involving the endocardium was a moderately large localized area of necrotic muscle cells showing cytoplasmic swelling, intense cytoplasmic staining with the eosin dye and fading and lysis of the nuclei unassociated with cellular inflammatory reaction. In an area beneath the endocardium where there was extensive degeneration of muscle cells and replacement fibrosis, numerous large and engorged sinuses of irregular or bizarre shapes lined with flattened endothelium meandered through the connective tissue (fig. 5). In another area small deposits of calcium occurred in the fibrous tissue.

Significant changes in the left atrium were extensive fibroelastic thickening of the endocardium, great engorgement of the capillaries and slight interstitial edema of the myocardium. No departures from normal were evident in the right ventricle except for a slight inflammatory reaction in the epicardium adjacent to the anterior portion of the interventricular septum.

Congestion, focal alveolar hemorrhages, slight edema, focal acute emphysema and massive areas of atelectasis were observed in the lungs.

Pathologic diagnoses. The pathologic diagnoses were as follows: anomalous origin of the left coronary artery from the pulmonary artery; extensive endocardial fibrosis, subendocardial degeneration and fibrosis of the myocardium; acute myocardial infarct; acute epicarditis; pronounced cardiac hypertrophy and dilatation (left ventricular); chronic passive congestion and moderate edema of the lungs; acute and chronic pulmonary emphysema; pulmonary atelectasis; slight hydrothorax bilaterally.

CASE 2.—*Summary.*—During the first two months of life, this infant had two protracted attacks of diarrhea. Not until the third month did the symptoms arising from the respiratory tract become predominant. The persistence of these symptoms together with the enlargement of the heart and the inversion of the T waves in the electrocardiogram led to the provisional diagnosis of a defect in a coronary artery. Necropsy showed the left coronary artery branching from the pulmonary artery. Endocardial fibrosis was extensive, and the myocadium just beneath the endocardium showed degenerative changes. Throughout the myocardium there were small infarcts and areas of fibrosis and calcification.

Details.—The patient was a white girl born prematurely July 29, 1944. The period of gestation was believed to be about seven and one-half months, and the birth weight was 4 pounds, 8 ounces (2,041 Gm.). Delivery was normal.

The father, 24 years of age, and the mother, 22 years of age, were both well. There had been no previous pregnancies.

The infant seemed normal at birth and was discharged from the hospital when she was 11 days old. Immediately after arriving home, she had diarrhea

and was readmitted to the hospital (Indianapolis), where she improved during a stay of one month. After discharge, she again had diarrhea, and two weeks later (September 19), when she was approximately 7 weeks old, she entered the Cincinnati Children's Hospital.

On admission, the infant weighed 5 pounds and 4 ounces (2,381 Gm.). Her temperature was 100 F., and she was moderately dehydrated. Her cardiac rate was rapid, but there were no murmurs or other evidence of cardiac disease. Laboratory examinations on admission showed 2,420,000 red cells per cubic millimeter, a hemoglobin value of 7.7 Gm. per hundred cubic centimeters and 11,100 white blood cells, with 42 per cent polymorphonuclear leukocytes, 50 per cent lymphocytes and 8 per cent large mononuclear cells. The Kahn reaction was negative. The urine was normal, the content of carbon dioxide was 10.3 volumes and that of chloride 129 milliequivalents per liter of plasma; the calcium content of the plasma was

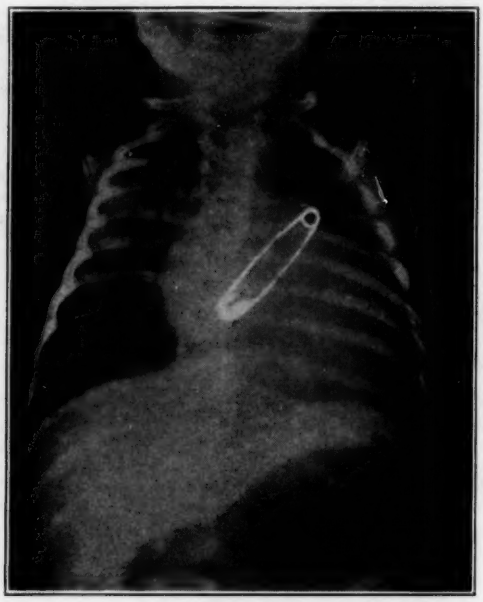

Fig. 6.—Roentgenogram of patient 2, taken Oct. 13, 1945, when patient was 2½ months old.

10.3 mg. per hundred cubic centimeters. Five stool cultures were negative for specific pathogenic organisms.

After the administration of sulfadiazine by mouth and of blood and fluids intravenously, the patient improved and was soon able to take food by mouth. After one week, the diarrhea subsided. The infant weighed 6 pounds and 12 ounces (3,062 Gm.). By this time the hemoglobin level had arisen to 14.3 Gm. per hundred cubic centimeters and the number of red cells to 4,400,000, but during the following week the respective values dropped to 10.9 Gm. and 3,300,000. Calcium levels of the blood fluctuated from 8.8 to 10.3 mg. per hundred cubic centimeters.

At 9 weeks, she had a nasal discharge, cough, vomiting and diarrhea, but no fever. The respiratory symptoms persisted, so that a roentgenogram of the chest was made (fig. 6). At this time gross enlargement of the heart was noted. In

the lung fields the bronchial markings were prominent. A teleoroentgenogram a few days later showed a cardiac width of 6.5 cm. in a chest 10.5 cm. wide. An electrocardiogram taken at this time showed slight inversion of the T waves in all leads (fig. 7).

Because of the persistent cough, respiratory difficulty, cardiac enlargement and inversion of the T waves in the electrocardiogram, the diagnosis of congenital anomaly of the coronary vessels was suspected. For a few days the infant seemed to improve but then suddenly became worse, the liver became larger, and she died on October 22, when she was approximately 3 months of age.

Necropsy: Gross examination. The thorax was symmetric and measured 10.5 cm. in greatest width. Each pleural cavity contained about 15 cc. of clear fluid. The pericardial sac was large, measuring 7.5 cm. transversely. It extended 5 cm. to the left of the midline and almost touched the left lateral wall of the chest. It contained approximately 5 cc. of clear fluid and was lined with a normal serous membrane. The thymus was normal.

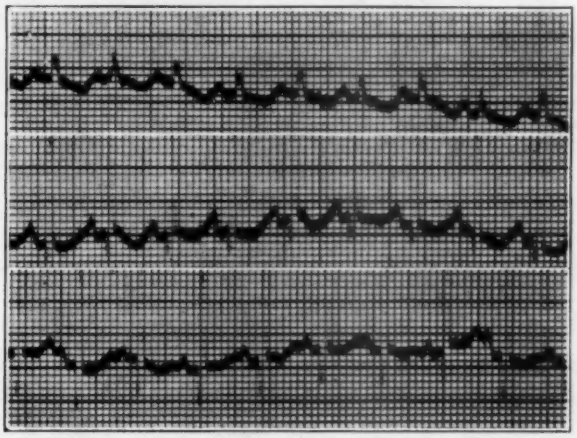

Fig. 7.—Electrocardiogram of patient 2 (taken when the patient was 2½ months old, on Oct. 17, 1945), showing inversion of T waves in all leads.

The heart was large and globular and weighed 43 Gm., approximately twice the normal weight (fig. 8). The great veins and arteries entered and emerged from the heart in normal positions. The cardiac valves were normal, and the cardiac septums were without defects.

The ostium of the left coronary artery measured 1 mm. in diameter and was located in the pulmonary artery behind the left posterior cusp of the pulmonary valve. From this point the artery curved to the left around the pulmonary artery and was divided into an anterior descending branch and a circumflex branch. The right coronary artery arose from the aorta behind the right cusp of the aortic valve and coursed over the posterior surface of the heart along the atrioventricular groove. Its ostium was small and measured only 0.5 mm. in diameter. The pulmonary artery and the aorta were otherwise normal, and there was no coarctation of the aorta. The ductus arteriosus was obliterated. The right atrium and the right ventricle were of average size, and were lined with a normal thin endocardium. The left atrium was also of average size, but its endocardium

was thick, white and opaque. The left ventricle, which formed the bulk of the heart, was hypertrophied and greatly dilated. Its walls varied in thickness from 2 mm. at the apex to 7 mm. near the base, and the endocardium, like that of the left atrium, was thickened, white and opaque.

The lungs were of average weight. Except for moderate congestion of the lower lobe of the left lung, the pulmonary tissue was elastic, pink, subcrepitant and moist. The tracheobronchial tree was normal. The abdominal viscera were congested but otherwise normal. The brain was not examined.

Microscopic examination. Extensive morphologic alterations were present in the left ventricle, particularly in the endocardium and subjacent myocardium (fig. 9). There was considerable fibroelastic thickening of the endocardium and vacuolation of the cytoplasm of the subjacent muscle fibers, many of which were isolated either singly or in groups by interlacing bands of fibrous tissue extending outward from the endocardium. The thebesian veins were prominent and possessed thick walls of fibroelastic tissue which was continuous with that of the endocardium.

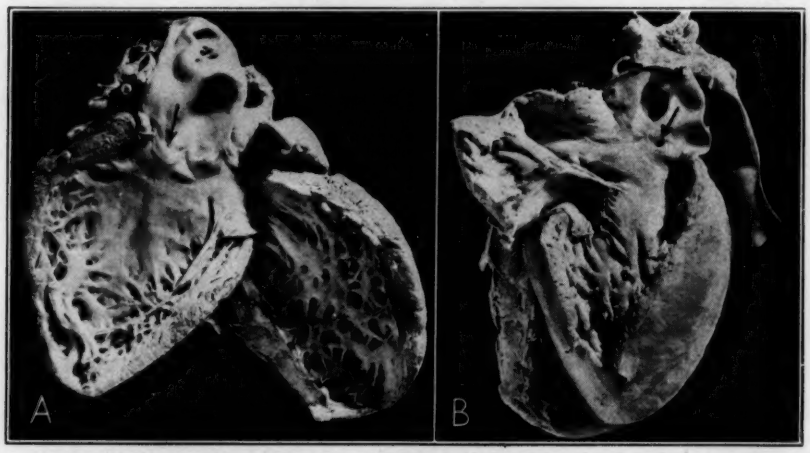

Fig. 8 (case 2).—*A*, hypertrophy and dilatation of the left ventricle; the tiny ostium of the right coronary artery may be seen behind the right cusp of the aortic valve. *B*, right ventricle; the ostium of the left coronary artery may be seen behind the left posterior cusp of the pulmonary valve.

Scattered deposits of calcium occurred in the areas of subendocardial fibrosis (fig. 9). There were hydropic degeneration of the papillary muscles and pronounced fibrosis of the covering endocardium. Evidence of active inflammation was absent in the endocardium except for a few areas where a slight lymphocytic reaction had occurred with an accompanying mild fibroblastic proliferation.

Numerous small areas where muscle cells had degenerated and had been replaced by connective tissue were observed in various portions of the left ventricle (fig. 10). In several regions there were large fibrous scars, one of which involved the entire left ventricular wall. In contrast to the attenuation, degeneration and vacuolation of many of the muscle cells in these regions, other muscle cells appeared hypertrophic and contained giant nuclei. Some of the areas of scarring were still moderately vascular and consisted of a cellular proliferating connective tissue infiltrated by a few leukocytes. In addition, a few small foci of polymorphonuclear leukocytes and lymphocytes unassociated with scarring were scattered throughout

the myocardium. Inflammatory reaction occurred in several of the subepicardial scars, but it was limited to aggregations of macrophages filled with blood pigment. The epicardium of the left ventricle was focally thickened and infiltrated by a few lymphocytes.

Fig. 9 (case 2).—Left ventricle; fibrosis of the endocardium and degeneration and fibrosis of the myocardium with deposition of calcium.

Morphologic changes in sections of the left atrium consisted of considerable fibroelastic thickening of the endocardium, vacuolation of the subendocardial muscle cells, moderate engorgement of the capillaries and moderate edema of the interstitial tissue.

The epicardium of the right ventricle was edematous and focally infiltrated by polymorphonuclear leukocytes and lymphocytes. There was general engorge-

ment of the capillaries, moderate edema of the interstitial tissue of the myocardium and slight to moderate vacuolation of the muscle fibers, particularly those beneath the endocardium. No fibrosis of the endocardium of the right side of the heart was present.

Significant pathologic changes in the other viscera consisted of passive congestion of the lungs, liver, spleen and kidneys, acute pulmonary emphysema, focal

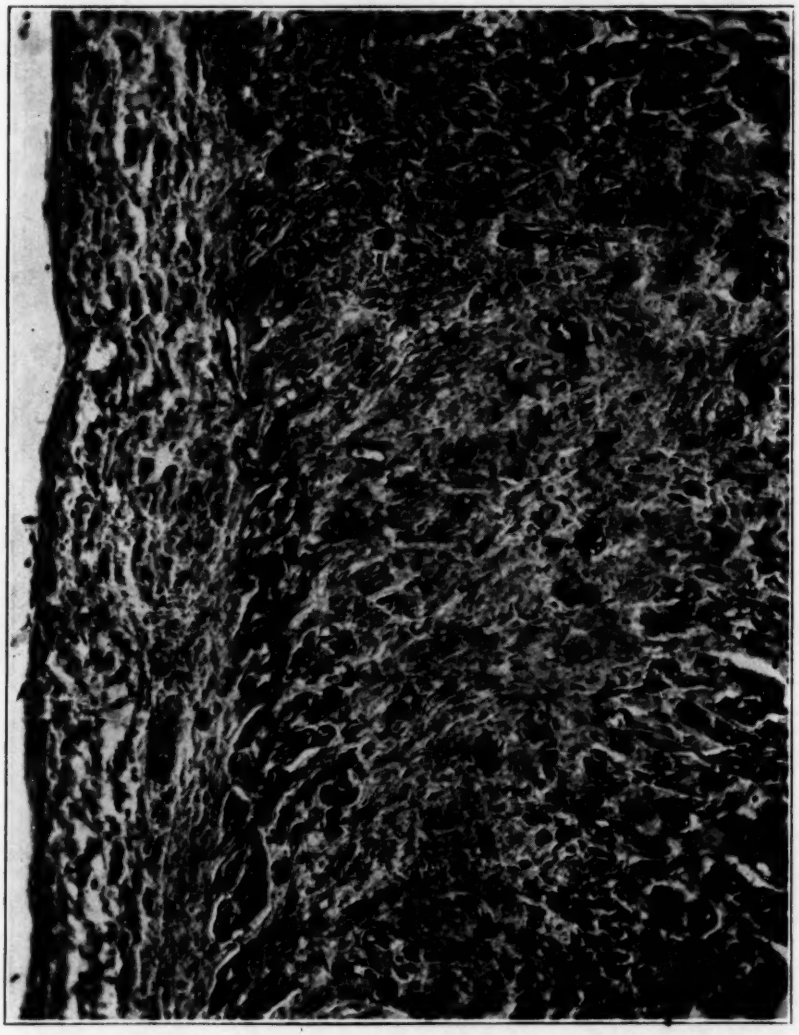

Fig. 10 (case 2).—Left ventricle; small organized subepicardial infarct.

pulmonary atelectasis, a slight amount of acute inflammatory reaction in the superficial layers of the mucosa of the stomach, ileum and colon and a few scattered areas of necrosis in the liver where lymphocytic and macrophagic reaction had taken place.

Pathologic diagnoses. The pathologic diagnoses were as follows: anomalous origin of the left coronary artery from the pulmonary artery; extensive endocardial fibrosis; subendocardial degeneration of the myocardium with fibrosis, calcification and multiple miliary infarcts in various stages of organization; focal acute and chronic epicarditis; pronounced cardiac hypertrophy and dilatation (left ventricular); chronic passive congestion of the lungs; slight bilateral hydrothorax; acute and chronic pulmonary emphysema and focal pulmonary atelectasis; acute passive congestion of the abdominal viscera; acute gastritis and enteritis; fatty infiltration of the liver.

COMMENT

There have been several excellent reviews [1] of the previously reported cases of anomalies of the coronary arteries, together with discussion of the causation. We have summarized this information and added a few facts learned from our own experience.

Incidence.—Anomalies of the coronary arteries were noted in 4 instances among 6,800 autopsies at the Massachusetts General Hospital [1b]; the condition occurred in 10 of the 1,000 patients with congenital heart disease reported on by Abbott.[2]

In a review of the cases reported in detail in the medical literature, Soloff [1c] found 16 instances in which the left coronary artery arose from the pulmonary artery and added 1 more case. Proescher and Baumann [3] described another. Our 2 patients bring the total to 20 cases.

Other types of anomalies of the coronary vessels have been reported less frequently, possibly because they produce less striking symptoms of cardiac disease. Only 2 individual reports of the right coronary artery's arising from the pulmonary artery were discovered by Soloff, but 8 of Abbott's 10 patients with anomalies of the coronary vessels had this defect. All these patients lived to adult life. The condition in which both coronary arteries have their origin in the pulmonary artery occurred in 2 patients of the group reviewed by Soloff. They both died within ten days after birth.

Other types of anomalous origin of the coronary vessels, which have been reviewed by Bland, White and Garland,[1b] are rare and apparently

1. (*a*) Sanes, L., and Kenny, F. E.: Anomalous Origin of Left Coronary Artery from Pulmonary Artery, with Myocardial Fibrosis of Left Ventricle and Partial Aneurysm at the Apex, Am. J. Dis. Child. **48**:113 (July) 1934. (*b*) Bland, E. F.; White, P. D., and Garland, J.: Congenital Anomalies of the Coronary Arteries: Report of an Unusual Case Associated with Cardiac Hypertrophy, Am. Heart J. **8**:787, 1933. (*c*) Soloff, L. A.: Anomalous Coronary Arteries Arising from the Pulmonary Artery, Am. Heart J. **24**:118, 1942.

2. Abbott, M. E.: Congenital Heart Disease, in Nelson's Loose Leaf Living Medicine, New York, Thomas Nelson & Sons, 1931, vol. 4, p. 207.

3. Proescher, F., and Baumann, F. W.: Abnormal Origin of the Left Coronary Artery with Extensive Cardiac Changes in a Female Child Thirteen Months Old, J. Pediat. **25**:344, 1944.

produce no characteristic symptoms. The coronary vessels may branch from higher than normal positions on the aorta or from the carotid or other arteries. Rarely, only one coronary vessel arises from the aorta and supplies branches to both the right and the left ventricle. The circumflex branch of the left coronary artery may have its origin in the pulmonary artery.

Embryology.—The coronary arteries appear as buds on the common arterial trunk at about the end of the second week of fetal life. Later, this common trunk divides into the aorta and the pulmonary artery. Bland, White and Garland concluded that the division may take place in an abnormal fashion or that the coronary artery buds may be situated in unusual locations so that one of them (or both) is left originating in the pulmonary artery instead of both in the aorta.

Pathology.—The pathologic changes occurring in the heart when the left coronary artery arises from the pulmonary artery have been similar in the majority of the cases reported. The left ventricle, supplied by venous blood under lower than average pressure, undergoes degenerative changes with necrosis of the muscle fibers and replacement by fibrous tissue. The degree of fibrosis of the myocardium has varied; occasionally there has been extensive scarring, and in some patients, including the 2 reported on by us, deposits of calcium have been noted in the myocardium. Infarcts in the myocardium and focal areas of epicarditis were noted in both our patients. Endocardial fibrosis has been a common finding and in most instances has been limited to the left side of the heart. The suggestion has been made that the lesions of the endocardium and the myocardium might be the result of fetal endocarditis, but it seems more likely that they are caused by an abnormal blood supply. Grossly and microscopically the pathologic changes resemble those produced by coronary occlusion in adults. In a recent review [4] of various forms of coronary occlusive disease in infants and children, infarcts of the myocardium were noted together with diffuse interstitial fibrosis of the myocardium, thickening of the subendocardial connective tissue and mural thrombi adherent to the endocardium.

Sinusoids, probably remnants of fetal structures, characterized by distended spaces lined with endothelial cells and full of blood, have been noted in the myocardium (Soloff) and even in the pericardial tissue (Proescher and Baumann). They occurred as a prominent feature in the subendocardial myocardium of our first patient. Dilatation of the left ventricle has been pronounced, and aneurysmal pouching sometimes occurred. Myocardial infarction and beginning pericardial adhesions were observed in our patients.

4. Stryker, W. A.: Coronary Occlusive Disease in Infants and Children, Am. J. Dis. Child. **71**:280 (March) 1946.

Symptoms and Signs.—In the previous reports, the infants usually appeared normal at birth, but within a few days or weeks, coughing, dyspnea and vomiting occurred in almost every instance. These symptoms seemed to be due primarily to pressure by the enlarged left ventricle on the lungs and the esophagus. They often subsided for a short period of time, only to recur with greater severity. In a few patients, the symptoms became worse when food was taken, but in others severe attacks occurred spontaneously. Some infants appeared to suffer from colicky pain, with episodes of dyspnea, sweating, pallor and apparent loss of consciousness which simulated attacks of angina pectoris experienced by adults.[1b,c]

The left side of the chest might bulge anteriorly, and in some cases retraction of the intercostal spaces was noted.[1a] The heart was greatly enlarged to the left, and roentgenograms sometimes demonstrated the unusual contour of a ventricular aneurysm. In lateral and oblique views the posterior enlargement of the heart and its encroachment on the esophagus might be demonstrated.

The first heart sound in the apical area was usually weak, the second sound in the pulmonic area often louder than normal. Rarely were any murmurs of consequence detected. No clubbing of the fingers was noted, and cyanosis was not present except during the paroxysmal attacks or in terminal stages of the disease.

On auscultation of the lungs, abnormal breath sounds and rales were frequently heard, predominantly on the left side, where compression of the bronchi and the lung by the large heart caused atelectasis or congestion. Pneumonia, pleural effusion and pericarditis with adhesions have been noted in different patients. Pericardial effusion has been suspected frequently but has not been found at necropsy.

In the first of our 2 patients, the respiratory symptoms were predominant and persisted throughout the entire six months of life. An area of opacity, noted first in the roentgenograms in the upper portion of the right lung, was probably due to atelectasis and possibly to a superimposed pneumonia. Whether this condition was caused by the large heart's pressing on a bronchus seemed doubtful, but a similar lesion which occurred later on the left side of the chest was unquestionably related directly to the cardiac pressure. Throughout her entire life the patient had respiratory distress without cyanosis. The second patient had recurrent gastroenteritis during the first two months of life which may have masked some of the early symptoms referable to the respiratory tract. Not until the third month was the attention of the physician called to the possibility of pulmonary or cardiac disease.

Electrocardiograms were published in only one of the previous reports, namely that of Bland and his co-workers. It showed an inversion of the T waves in all leads but most pronounced in leads I and II.

The QRS complexes were low in amplitude. In the first patient reported here, the T wave was inverted only in the first lead, and there was no axis shift or decrease in the amplitude of the QRS. In the second patient the inversion of the T wave occurred in all leads.

Prognosis.—The majority of patients with the left coronary artery arising from the pulmonary artery have died in infancy, the youngest at 2½ months and the oldest at the age of 13 months (the patient of Proescher and Baumann). Four patients with similar lesions have lived to adult life, their ages at the time of death varying from 27 to 64 years. One of the adults died suddenly, apparently of cardiac failure, and 2 others suffered from angina pectoris for a number of years before death. Cardiac failure therefore seemed to be a contributing cause of death in 3 of the 4 adult patients.

SUMMARY

The histories of 2 infants with anomalous origin of the coronary arteries recorded here bring the total number of reported cases to 20. In both cases enlargment of the heart, persistent symptoms of respiratory distress and the inversion of the T waves in the first lead or in all leads of the electrocardiogram permitted a tentative clinical diagnosis of the nature of the cardiac disorder.

In the pathologic examination in both cases the important abnormalities found, other than the origin of the left coronary artery from the pulmonary artery, were limited to the left ventricle, where there were endocardial fibrosis, degenerative changes of the myocardium with replacement by fibrous tissue, infarcts in the myocardium and in 1 case persistence of embryonic sinusoids.

STAPHYLOCOCCIC (SUPPURATIVE) PNEUMONIA IN INFANCY AND IN CHILDHOOD AND ITS SURGICAL ASPECTS

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UNTIL a few years ago pneumonia in childhood caused by the staphylococcus was regarded as nonexistent or was referred to casually in the literature as a variant with an extremely high mortality. The subject has recently received consideration by a number of authors, who have also stressed this high mortality. This increased interest in staphylococcic pneumonia probably can be ascribed to an increasing emphasis on etiologic diagnosis. It has become apparent that because of therapeutic considerations differentiation between the various types of pneumonia on an etiologic basis may be of greater import than that based on clinical or anatomic features.

This communication is based on observations of 40 [1] proved cases of bronchogenous staphylococcic pneumonia seen during a period of more than fifteen years. We have excluded from this study all cases of staphylococcic sepsis with metastatic pulmonary abscesses. We shall propose a concept of the pathogenesis, outline the pathology, classify and describe the clinical manifestations, present the roentgenologic features and stress certain therapeutic implications which, it is hoped, will contribute to the lowering of the mortality rate of the disease.

The literature on staphylococcic pneumonia is not large. A brief review can begin with the isolation by Fraenkel [2] in 1904 of the staphylococcus from the lung in a fatal case of pneumonia. Chickering and Park [3] in 1919 described a large number of cases of staphylococcic pneumonia in adults observed during the course of an influenza epidemic.

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1. Since this paper was completed, 10 more cases have been encountered. They will not be included because they present no additional clinical features. However, 1 will be referred to as illustrative of the specific effect of penicillin on the disease.

2. Fraenkel, A.: Spezielle Pathologie und Therapie der Lungenkrankheiten, Berlin, Urban & Schwarzenberg, 1904, pp. 340, 534 and 536.

3. Chickering, H. T., and Park, J. H., Jr.: Staphylococcus Aureus Pneumonia, J. A. M. A. **72**:617 (March 1) 1919.

Reports by MacGregor[4]; Cohen[5]; Kanof, Kramer and Carnes[6]; Clemens and Weens[7]; Genninger,[8] and McBryde[9] have appeared in the pediatric literature. Kanof, Kramer and Carnes[6] presented a valuable statistical analysis of staphylococcic pneumonia including 25 cases of the primary variety. In their report the clinical features and the pathology and bacteriology were discussed.

ETIOLOGY

The frequency with which the staphylococcus can be shown to be the etiologic organism in pneumonia varies with different age groups, infants being apparently far more susceptible to invasion by this organism than older children or adults. Many attempts have been made to separate pathogenic from other strains of staphylococci.[10] There seems to be some relationship between pigment and toxin production, on the one hand, and pathogenicity, on the other. Staphylococcus aureus alpha is the most common pathogenic form, Staphylococcus albus being only occasionally endowed with pathogenic properties. However, the occasional pathogenicity of Staph. albus cannot be overlooked. In 5 of our cases it was shown to be the etiologic agent, examinations of empyema fluid consistently revealing pure cultures of this organism.

Concerning the incidence or, indeed, the existence of staphylococcic pneumonia, attention must be directed to the conflicting criteria for the diagnosis which are set up by different authors (diagnosis by cultures of material from the throat and of sputum, postmortem examination and other means). Isolation of the organism in pure culture directly from the lung at postmortem examination, at operation or on occasion by direct pulmonary puncture comprises definitive proof of its etiologic significance. Similarly, if the pleural cavity is invaded and the staphylococcus in pure culture is isolated, the diagnosis is established. The isolation of the staphylococcus from the nose and throat of an infant or child is not evidence of the existence of staphylococcic pneumonia. Indeed, the culture of material from the throat has been of little aid in our experience. In only 1 case (case 26) of staphylococcic pneumonia was a pure culture of Staph. aureus obtained from the throat early in the disease. Cultures of material from the throat positive for the staphylococcus late

4. MacGregor, A. R.: Arch. Dis. Childhood **11**:195 (Aug.) 1936.

5. Cohen, P.: M. Clin. North America **22**:1473, 1938.

6. Kanof, A.; Kramer, B., and Carnes, M.: J. Pediat. **14**:72, 1939.

7. Clemens, H. H., and Weens, H. S.: J. Pediat. **20**:281, 1942.

8. Genninger, L. E.: Arch. Pediat. **60**:419, 1943.

9. McBryde, A.: Hemolytic Staphylococcus Pneumonia in Early Infancy: Response to Penicillin Therapy, Am. J. Dis. Child. **68**:271 (Oct.) 1944.

10. Gay, F. P., and others: Agents of Disease and Host Resistance, Springfield, Ill., Charles C Thomas, Publisher, 1935, p. 504.

in the disease are seen in cases of spontaneous rupture and drainage of a pulmonary abscess by way of the bronchial tree. The incidence of such cultures is no greater in staphylococcic pneumonia than in quite unrelated conditions. These observations are in agreement with those of Hallman [11] and of Alexander and others.[12] Among adults the culture of material from the throat apparently is of greater value.[13]

INCIDENCE

The proportion of staphylococcic pneumonia to other pneumonias of infants and children varies from 1 to 8.5 per cent.[14] The staphylococcus has been recovered from 10 to 15 per cent of all children suffering from acute empyema. [15] Neuhof and Berck [16] pointed out that in infancy Staph. aureus is the preponderant organism in the pleura in cases of empyema.

An analysis of the seasonal incidence of our cases of staphylococcic pneumonia reveals a curve with the greatest peak in the fall and winter months and with a precipitous decline during the spring and summer months. This seasonal incidence is similar to that reported by Kanof and others,[6] and does not differ from that seen in other forms of pneumonia.

RELATIONSHIP TO VIRUS INFECTIONS

In certain years and in specific localities the incidence of staphylococcic pneumonia rises abruptly. This increased incidence usually coincides with an epidemic of influenza. The question of an association between primary virus respiratory disease and staphylococcic pneumonia was discussed by Chickering and Park [3] in their study made during the course of a severe epidemic of influenza in an army camp in 1919. They observed influenza in 1,800 patients, in 1,400 of whom pneumonia developed. Of this group, 385 died, and at postmortem examination Staph. aureus was isolated from the lungs of 153. Since that

11. Hallman, F. A.: Proc. Soc. Exper. Biol. & Med. **36**:789, 1937.

12. Alexander, H. E.; Craig, H. R.; Shirley, R. G., and Ellis, C.: J. Pediat. **18**:31, 1941.

13. Reimann, H. A.: Primary Staphylococcic Pneumonia, J. A. M. A. **101**:514 (Aug. 12) 1933.

14. Carey, B. W., and Cooley, T. B.: J. Pediat. **15**:613, 1939. Spence, R. C.: Empyema in Infants and Young Children, Am. J. Dis. Child. **20**:545 (Dec.) 1920. Menten, M. L.; Bailey, S. F., and DeBone, F. M.: J. Infect. Dis. **51**:254, 1932. Lyon, A. B.: Bacteriologic Studies of Pneumonia and Post-Pneumonic Empyema, Am. J. Dis. Child. **23**:72 (Jan.) 1922.

15. McEnery, E. T., and Brennemann, J.: Aspiration in the Treatment of Empyema in Children, Am. J. Dis. Child. **44**:742 (Oct.) 1932. Hochberg, L. A., and Kramer, B.: Acute Empyema of Chest in Children, ibid. **57**:1310 (June) 1939.

16. Neuhof, H., and Berck, M.: Staphylococcic Empyema and Pyopneumothorax, Arch. Surg. **30**:543 (March) 1935.

time several authors have suggested that the staphylococcus may act in symbiosis with a virus or that the virus may prepare the way for the subsequent secondary invasion by pyogenic organisms.[17]

Scadding [18] in 1937 was the first to demonstrate in the human being the coexistence of the staphylococcus and a virus. He reported a case of fulminating influenzal pneumonia which was fatal on the third day. The culture of the lung revealed Staph. aureus in great numbers, and the virus of influenza also was isolated. Stokes and Wolman [19] in 1940 reported a case in which they too were able to isolate the virus of influenza and Staph. aureus from the lung. Finland, Strauss and Peterson [20] and Michael [21] in a recent epidemic of influenza in Boston demonstrated the etiologic significance of the influenza virus by neutralization tests in a number of cases of staphylococcic pneumonia. On analyzing the clinical data of our cases, it appears that in 6 instances the pulmonary disease was apparently a complication of an existing virus infection. In addition, we observed 2 patients in whom the clinical course and the postmortem picture were typical of those seen in staphylococcic pneumonia complicating epidemic influenza. From the foregoing data it is apparent that occasionally a virus infection may precede or be associated with a staphylococcic invasion of the lung.

PATHOGENESIS

The term staphylococcic pneumonia should be reserved for that form of suppurative bronchopneumonia in which bronchogenous invasion of the lung is presumed to have taken place. Since the picture would be confused if metastatic staphylococcic abscess of the lung were considered, all forms of hematogenous staphylococcic invasion of the lung have been excluded.

Studies made at autopsy and experiments dealing with the reproduction of the disease indicate that the infection descends from the upper respiratory passages and progressively involves the trachea and bronchi. It then extends by way of the lymphatics and the interstitial tissues to reach the pulmonary parenchyma. The extension by bronchial pathways accounts, first, for the peripheral location in the lung of

17. McCordock, H. A., and Muckenfuss, R. S.: Am. J. Path. **9**:221, 1933. Baker, R. D.: South. M. J. **35**:240, 1942.

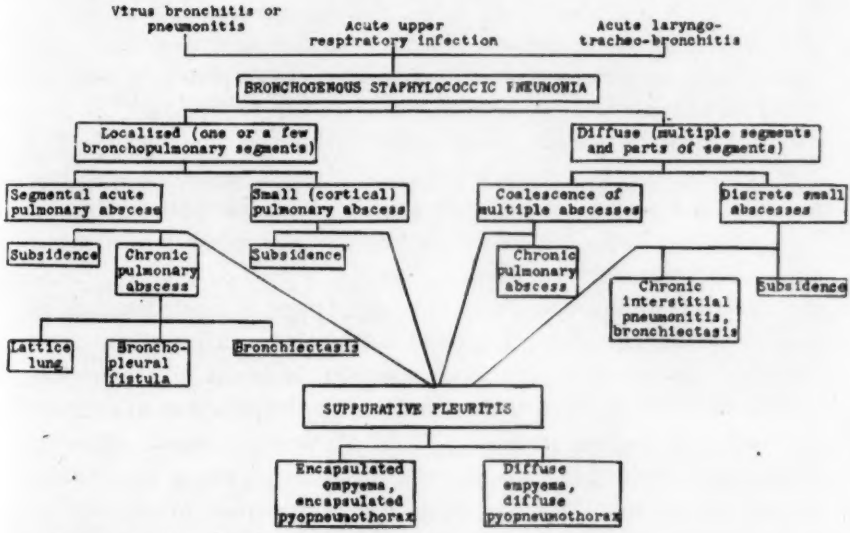
18. Scadding, J. G.: Quart. J. Med. **6**:425, 1937.

19. Stokes, J., Jr., and Wolman, I. J.: Internat. Clin. **1**:115, 1940.

20. Finland, M.; Strauss, E., and Peterson, O. L.: Tr. A. Am. Physicians **56**:139, 1941. Finland, M.; Peterson, O. L., and Strauss, E.: Staphylococcic Pneumonia Occurring During Epidemic of Influenza, Arch. Int. Med. **70**:183 (Aug.) 1942.

21. Michael, M., Jr.: Staphylococcus Aureus Pneumonia with Special Reference to Its Occurrence as a Complication of Influenza, J. A. M. A. **118**:869 (March 14) 1942.

the suppurative lesion and, second, for the segmental distribution of the pathologic process. In connection with the latter, it was first established by Glass [22] that each lobe of the lung may be subdivided into anatomically distinct bronchopulmonary segments. A segment consists of a bronchus and its associated parenchyma, the bronchus being one of the main divisions of a lobar bronchus. These bronchopulmonary segments are somewhat cone shaped, with the periphery of the cone extending to the surface of the lung. Thus, almost all segments are in contact with the parietes. Since this segmental feature which is so characteristic of bronchogenous spread has not been previously pointed out with regard to staphylococcic pneumonia and since we deem it to be of considerable



A concept of pathogenesis and pathology.

In the diagram, the localized infections of the pleura are placed on the side of the localized type of staphylococcic pneumonia because they occur as complications of localized pulmonary lesions in the majority of cases. Similarly, the diffuse pulmonary infections and nonlocalized pleural complications are placed together. The diagram applies in general to suppurative pneumonia due to other aerobes.

clinical significance, we wish to stress the fact that segmental involvement is frequently encountered when the opportunity for a complete examination (autopsy) exists. At postmortem examination there is often, in addition, evidence of direct spread from the bronchi to the pulmonary parenchyma. Furthermore, bronchial fistulas have been demonstrated in the great majority of our cases of staphylococcic

22. Glass, A.: Am. J. Roentgenol. **31**:328, 1934.

empyema or of pulmonary abscess at operation, after operation or at postmortem examination. This is cogent evidence that the pathway of infection is bronchogenous. In contrast, a pulmonary lesion of hematogenous origin only rarely leads to a bronchial fistula. Necrosis of the wall of a bronchus of substantial proportions is exceptional under such circumstances and, when it does occur, can be regarded as an accident.

PATHOLOGY

The cases of staphylococcic pneumonia may be divided on a pathologic basis into two groups: those in which suppuration plays a minor role, as in the acute fulminating cases when abscesses have little time to form, and those in which suppuration is prominent. In our series there was no instance in which the disease was too fulminating for abscess formation. However, MacGregor [4] has described such cases occurring in early infancy. When suppuration takes place, the abscesses are often multiple and arranged in clusters about bronchioles. At times they may coalesce to form a large solitary pulmonary abscess. The location of these abscesses in the periphery of the lung and their restriction to bronchopulmonary segments are features of considerable significance. Thus, empyema or pyopneumothorax secondary to rupture of a pulmonary abscess is a frequent complication. There is a decided tendency toward the formation of adhesions, with the development of loculations and the walling off of staphylococcic pleural infections. Invasion of the entire pleural cavity is noted only when a sudden blow-out of a pulmonary abscess develops or when the air and pus in the pleura is so extensive and under such great tension as to break through pleural adhesions. It has been suggested [18] that in some instances an initial virus disease acts as a descending infection of the respiratory tract, which may stop short at any level. If a secondary bacterial invasion occurs, the influenza-like lesions become complicated by the effect of this invasion with pyogenic organisms.[23] The principal lesions of the respiratory tract regarded as influenzal are extensive and may cause severe injury to the bronchi and bronchioli with desquamation and necrosis of epithelium; exudation into the interstitial, peribronchial and perivascular tissues; focal necrosis of alveolar walls, and intra-alveolar hemorrhage. This corresponds to the hemorrhage, edema and necrosis seen by McCordock and Muckenfuss [17] in their experimentally produced hemorrhagic pneumonia. Superimposed on this lesion one notes varying degrees of suppuration, characteristic of invasion by pyogenic organisms. The pathology of fulminating staphylococcic bronchopneumonia is well portrayed in the following case.

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23. Wollenman, O. J., and Finland, M.: Am. J. Path. **19**:23, 1943.

CASE 7.—W. Y., a 10 year old boy, died after an illness of about twenty hours' duration. This illness began with fever and sore throat and was rapidly followed by hoarseness and progressively increasing respiratory distress. Shortly after the onset the patient complained of pain in the right axilla. On his admission to the hospital, respiratory distress was extreme. Roentgen examination of the chest revealed evidence of a bronchopneumonic infiltration in the right lung extending from the level of the second rib to the diaphragm. Despite oxygen therapy and administration of stimulants, the patient died within twenty hours of the onset of symptoms. Postmortem examination revealed a necrotizing tracheitis and bronchitis. Overlying the visceral pleurae was a thin fibrinous exudate. Both lungs were firm and fleshy. There was no crepitation except in a small area at the base of the upper lobe of the left lung. In the right lung, principally in the lower lobe, there were several small circular yellowish areas, somewhat raised above the surface. In a cut section all the lobes presented an almost identical appearance. Large, rather well demarcated, somewhat irregular hemorrhagic areas were present. These were slightly raised, firm and granular. They were not infrequently triangular, with their apexes toward the hilus. A number of these areas, usually smaller, were decidedly more granular and demonstrated central necrosis. Interspersed among these firm areas were rather well circumscribed, grayish purulent foci, many of which lay immediately beneath the pleura. Within the lower lobe of the right lung was a conglomerate mass of such purulent material. Culture of material from the pulmonary abscess and culture of the pleural exudate both revealed a pure growth of Staph. aureus.

The foregoing description of the pathologic changes of staphylococcic pneumonia corresponds, in general, to the picture reported by Neuhof and Thomas [24] in cases of suppurative bronchopneumonia caused by a variety of pyogenic aerobes.

CLINICAL FEATURES AND CLASSIFICATION

Analysis of our cases of staphylococcic pneumonia reveals a diversity in the clinical manifestations such as cannot be deduced from the reports dealing with single isolated instances or with small groups of cases of this disease. Review of the case histories here presented suggests a classification into (1) an acute diffuse, (2) an acute localized and (3) a subacute and chronic variety. The following description will take up these groups and subgroups, our chief purpose being to set forth certain features which have therapeutic implications.

CLINICAL CLASSIFICATION OF STAPHYLOCOCCIC PNEUMONIA

I. Acute diffuse suppuration
   A. Little or no pleural involvement (8 cases)
   B. Widespread pleural involvement (11 cases)
      1. Generalized empyema
      2. Generalized pyopneumothorax

24. Neuhof, H., and Thomas, A.: Acute Suppurative Bronchopneumonia, Arch. Int. Med. **75**:45 (Jan.) 1945.

II. Acute localized suppuration (17 cases)
  A. Acute pulmonary abscess
  B. Encapsulated empyema
  C. Encapsulated pyopneumothorax
III. Subacute and chronic (4 cases)

I. *Acute Diffuse Suppuration.*—A. Little or No Pleural Improvement: The acute diffuse form of the disease in which there is rapid evolution of the pulmonary lesion with little or no pleural involvement is the most fulminating variety and is a rapidly fatal illness except in those cases in which the patient responds to treatment with penicillin. The pulmonary lesion is usually widespread, with involvement of many scattered bronchopulmonary segments and with little or no evidence of localization of the pathologic process. The condition can be subdivided into (1) the nonepidemic and (2) the epidemic type. The nonepidemic form is usually seen in very young infants (our youngest patient was 9 days old). This age incidence conforms with the prevalent statistics, which show that infections with Staph. aureus in very young infants are exceptionally virulent and fatal.[25] Clinically, differentiation is impossible between this group of infections and bronchopneumonia due to other invading organisms. Fever, cough and dyspnea are present, and physical and roentgen examinations of the chest reveal areas of consolidation. The clinical course of the illness is rapidly downhill, the patient usually dying before extensive pleural complications occur. The average duration of the illness in our patients was four to five days. Postmortem examination revealed either disseminated abscesses or clusters of abscesses in several bronchopulmonary segments and limited, if any, pleural involvement.

The acute diffuse epidemic form of this disease is most often seen as an apparent complication of influenza. It may attack persons of any age and has a very rapid course. There were 2 cases in our series, in both of which death occurred in twenty-four to forty-eight hours. The patients are overwhelmed by toxemia, and a necrotizing tracheobronchitis adds to their distress. Pulmonary suppuration is present, but the toxemia terminates the illness before pleural invasion occurs. This condition closely simulates the virulent form of influenza seen in epidemics.

B. Widespread Pleural Involvement: In the acute diffuse form of this disease in which the rapid pulmonary evolution is accompanied with a widespread pleural infection, there is little tendency toward localization of the process. This, too, is a rapidly progressing infection, 6 of 11 cases in our series having terminated fatally. The average age of the 11 patients was 2½ years. The average duration of symptoms prior to

25. Lichty, J. A.; Katsampes, C. P., and Baum, W. S.: J. Pediat. **22**:549, 1943. Ladd, W. E., and Swan, H.: ibid. **23**:297, 1943.

development of the pleural complication was seven to eight days. In all these cases of widespread pulmonopleural involvement the pleural invasion was due to a ruptured pulmonary abscess. The initial clinical picture is that of a bronchopneumonia, which may or may not appear to be unusually severe. The development of pulmonary suppuration is insidious and does not apparently reflect itself clinically. Then there is the abrupt and dramatic change in the condition of the patient due to the perforation of a pulmonary focus. Dyspnea and cyanosis become extreme, and there rapidly develops a state of shock. Unless this complication is borne in mind, its existence sought for and appropriate surgical intervention promptly applied, all or almost all these patients will die. Other authors report almost uniform fatality in cases of this type in which there is not prompt surgical intervention. All 11 patients in our series were operated on as presenting surgical emergencies, at which time a stab thoracotomy with under-water drainage was done. Either because the operation was too long delayed or because pleural drainage had little effect on the spreading suppuration within the lung, recovery occurred in only 4 of 11 cases. In all, however, the effects of mediastinal displacement were relieved, death from this cause being prevented. Thus, emphasis should be placed on the fact that occasional recoveries will follow timely surgical intervention even in this group of cases in which because of the widespread involvement the condition is not usually regarded as suited for surgical intervention.

II. *Acute Localized Suppuration.*—Staphylococcic suppurative pneumonia is confined to a single or to adjacent bronchopulmonary segments. Suppuration takes place within an area of consolidation, with the formation of either a single pulmonary abscess or multiple abscesses, which may coalesce to form a single segmental abscess. The abscess may subside, rupture into the pleura or persist and become a chronic pulmonary abscess. Because of its peripheral location, rupture into the pleural space may occur at any time with the development of a suppurative pleuritis. During the stage at which there is impending rupture of the pulmonary focus, pleural adhesions are increasingly formed. The resultant empyema or pyopneumothorax is encapsulated. The pleural lesion may be situated at any point in the general pleural space or may be interlobar, depending on the site of the underlying pulmonary focus. During the stage of bronchopneumonia the signs and symptoms are not distinctive of suppuration except in rare instances in which pus is expectorated. With the development of a localized suppurative pleuritis, there usually is an increase in dyspnea and the development of dulness to percussion. Mediastinal shift and the classical signs of pneumothorax do not develop as a rule because of the localized nature of the lesion and the partial fixation of the mediastinum. At this stage the problem requires surgical inter-

vention, and an excellent result may be anticipated following adequate surgical management. If the indications for surgical treatment are overlooked or if the drainage is inadequate, the course of the illness is one of progression. When there is increasing tension within the localized pleural lesion, rupture through the adhesions occurs with a resultant generalized suppurative pleuritis. Occasionally the acute process subsides, and a subacute or chronic empyema ensues.

A complication of inadequate drainage or of nonsurgical treatment of an acute staphylococcic pulmonary abscess is the spread of the infection from the involved portion of the lung to adjacent or even remote bronchopulmonary segments by the mechanism of bronchogenous spillover. A less obvious complication, and one of considerable importance in later life, is the apparently spontaneous cure of the abscess, with the development of an insidious chronic abscess with or without bronchopleural fistula. We have seen a number of cases in which the pulmonary abscess appeared healed after the acute episode in early childhood but was followed after a considerable interval by the symptoms of pulmonary abscess. Whenever there has been an opportunity to inspect roentgenograms taken during the acute episode, it has been found that the abscess of later life is at the site of the original lesion. It can be said in passing that most of the abscesses dating from infancy or childhood require for their cure not only extensive but also hazardous operative procedures. All this gives point, we believe, to the argument we advance in favor of operating on the abscess in the acute stage (within six weeks of onset), if necessary, or in any event of not discharging a patient, even if entirely symptom free, in the presence of a roentgenographically demonstrable cavity.

PHYSICAL EXAMINATION

The physical examination of the chest in cases of staphylococcic pneumonia reveals signs which are dependent on the phase of the disease. Early in the illness there are the signs of pulmonary consolidation. With progression of the syndrome and the development of a pulmonary abscess, one might anticipate changes in the physical signs which would lead to the correct diagnosis. However, the signs are not distinctive, and the diagnosis of pulmonary abscess must of necessity rest on the roentgen examination, or at times in older children on the sudden expectoration of a quantity of pus. With the development of a localized empyema or pyopneumothorax there may be noted gradually increasing dyspnea. It is impossible to differentiate between a localized empyema and a localized pyopneumothorax by physical signs alone. If one notes increasing dyspnea associated with dulness to percussion, one should strongly suspect the presence of a pleural complication. In cases of extensive, and particularly of nonencapsulated, pyopneumothorax, there

is often the dramatic change already referred to, due to shifting of the mediastinum and tension within the infected space. Dyspnea and cyanosis become severe. Diminished excursions of the chest are noted, and bulging of the interspaces may be present. On percussion there are hyperresonance above and flatness below, the extent of each depending on the relative amounts of fluid and air within the pleural cavity. The most consistent physical sign of pyopneumothorax in children, however, is the diminution in the intensity or the complete absence of the breath sounds over a large area of the affected lung. A succussion splash or coin sound is rarely encountered.

The associated gastrointestinal symptoms are of frequent occurrence and often of considerable importance. Our observations are in accord with those of Kanof and others[6] who have expressed the belief that gastrointestinal symptoms are more prominent in staphylococcic than in pneumococcic pneumonia. Abdominal pain, vomiting, diarrhea and abdominal distention have all been noted. In our series severe abdominal distention was present in a majority of the patients and proved to be serious in not a few because of the resultant limitation of the pulmonary excursions. In several instances the prominent gastrointestinal symptoms led to difficulty in diagnosis. One child was admitted to the hospital with a diagnosis of acute appendicitis; in several, the question of primary peritonitis was entertained and abdominal puncture was employed as an aid in diagnosis, and in 1 infant the abdominal symptom complex was so outstanding that a roentgenogram of the chest was never obtained and the correct diagnosis was ascertained only at postmortem examination.

THE WHITE BLOOD CELL COUNT

The white blood cell counts ranged from 3,700 to 75,000 per cubic millimeter. Two patients with the influenzal type of the disease had a leukopenia even when suppuration existed within the lung. The tendency in the majority was toward leukocytosis, usually of a substantial degree. The average white blood cell count for the entire group was 20,700. Only 6 patients had white cell counts of less than 10,000. There was no significant correlation between the leukocytic response and the prognosis. One patient with a white cell count of 3,800 and another with a white cell count of 75,000 recovered. A fatal outcome was observed in a patient with a count of 33,700 white blood cells and in one with a count of 3,700.

ROENTGENOGRAPHIC FEATURES

The roentgenographic features of staphylococcic suppurative pneumonia are often distinctive, but they are not pathognomonic. Neuhof

and Touroff have called attention to the one roentgenographic feature [26] which is characteristic of all suppurative pneumonias, namely, the appearance of one or more areas of rarefaction in the midst of pneumonic infiltration. Laminagrams may be necessary to reveal such areas in adults, but often ordinary roentgenograms (perhaps somewhat overexposed) will suffice for infants and young children. The characteristic areas of rarefaction are visible sooner or later in the great majority of cases of staphylococcic pneumonia in childhood. They are more commonly encountered than in suppurative pneumonias associated with mixed bacterial flora. Sometimes they appear in a rontgenogram taken a day following one which did not reveal any area of rarefacton. This feature is emphasized because its presence virtually proves the pneumonia to be caused by the staphylococcus when it is encountered in an infant and makes the diagnosis probable when it is encountered in a young child.

Other roentgenographic features of staphylococcic pneumonia are, first, shadows corresponding to infiltrations about bronchi, blood vessels and interlobular septums; second, changes indicating the presence of focal, segmental or even lobar types of atelectasis; third, densities of lobular, segmental or lobar type. Various combinations of these features may produce most bizarre and at times confusing images.

Perhaps the most important clinical aspect of the roentgenologic picture of staphylococcic pneumonia is the rapidity with which changes in the roentgenograms of the chest occur. Thus on one day a roentgenogram may reveal an area of rarefaction in the midst of pneumonic infiltration, and on the next day a large collection of fluid and air in the pleura may completely obscure the pulmonary lesion. In other instances a homogeneous density noted in a roentgenogram may be followed shortly by the appearance of a pulmonary cavity with fluid level. In still other cases a collection of fluid and air with displacement of the mediastinum may comprise the first roentgenologic evidence that the pulmonary lesion is not a simple pneumonic one. At times there is the problem of differentiating between a suppurative lesion which is still confined to the lung (pulmonary abscess) and one which has already invaded the general pleural or an interlobar space. These remarkably sudden changes in the roentgenogram are of considerable importance, since they may occur in the presence of an unchanging clinical course. The sudden rupture of a pulmonary focus into the general pleural space usually produces decidedly characteristic manifestations. It is surprising, however, how often less diffuse pleural invasions occur which are registered roentgenologically without corresponding clinical manifestations. Only by frequent roentgenograms can these clinically significant changes be

26. Neuhof, H., and Touroff, A. S. W.: Surgery 4:5, 1938.

discovered. The taking of roentgenograms at judiciously spaced intervals can play an important part in contributing to an understanding of the development of the disease and of the therapeutic indications.

TREATMENT

Medical.—General supportive treatment with the administration of oxygen and adequate quantities of fluid as well as transfusions of blood or plasma is as useful for staphylococcic as for other pneumonias. Gastric and intestinal distention at times require almost continuous treatment for their control.

In contrast to the dramatic results obtained in nonsuppurative pneumonias, therapy with sulfonamide compounds has been disappointing in staphylococcic pneumonia. Indeed, it is difficult at this time to be certain of any beneficial effect from such therapy. The animal experiments of Kolmer and Brown [27] led these workers to conclude that in the sulfonamide therapy of staphylococcic infections in general, both sulfathiazole and sulfapyridine possessed some therapeutic activity, sulfathiazole being of greater value than sulfapyridine.

The in vitro studies of Finland, Strauss and Peterson [20] showed sulfathiazole to possess the most bacteriostatic effect of the drugs studied, while sulfadiazine was of less value than sulfathiazole but was considerably more effective than sulfapyridine. The reports in the literature of the results of sulfonamide therapy of staphylococcic pneumonia are exceedingly difficult to evaluate because of (1) the comparatively few patients treated, (2) the absence of detailed accounts of the individual patients treated and (3) the failure to evaluate other therapeutic measures, both medical and surgical. Carey and Cooley [28] in 1939 reported on the use of sulfapyridine in the pneumonias of infancy and childhood. A staphylococcus was found to be the causative organism in 6 of their patients. All received intensive treatment with sulfapyridine; blood levels of 12 to 20 mg. per hundred cubic centimeters of free sulfapyridine were maintained. The fatality rate was 100 per cent. Carey [29] continued this study and in 1941 reported an additional series of cases. In this group there were 15 cases in which a staphylococcus was thought to be the causative agent. Eight of the patients were treated with sulfapyridine, and all died. Seven patients were treated with sulfathiazole, and only 2 died. The lower fatality rate for the sulfathiazole-treated patients was encouraging, but unfortunately no mention was made as to the effect, if any, of other forms of treatment.

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27. Kolmer, J. A., and Brown, H.: Chemotherapy and Chemoserotherapy of Staphylococcic Infections, Arch. Int. Med. **69**:636 (April) 1942.

28. Carey, B. W., and Cooley, T. B.: J. Pediat. **15**:613, 1939.

29. Carey, B. W.: J. Pediat. **18**:153, 1941.

In our series there were 9 patients treated with adequate doses of sulfonamide compounds. Five of these patients were treated with sulfapyridine. Administration of the drug was started early in the disease, and adequate dosage (at least 1.5 grains per pound [0.195 Gm. per kilogram] per day) was maintained. In this group there was only 1 fatality. Yet it was felt that the sulfapyridine was of no definite effect in these cases. In all 4 patients who survived the clinical course of the disease was progressive despite administration of sulfapyridine, but rapid cure followed surgical intervention. In the fatal case the disease progressed and the patient was not operated on. One of our patients was treated with both sulfapyridine and sulfathiazole, and 2 were treated with sulfathiazole and sulfadiazine. All 3 of these patients required surgical intervention to obtain a cure, and the effect of the sulfonamide therapy was certainly not striking in any instance. In 1 case in which the patient was treated with sulfathiazole, it was felt that the drug did influence the course of events, and a clinical cure was obtained without surgical intervention (case 31, V.A., described in the following case reports).

Treatment with penicillin was employed by us in only a few verified cases of staphylococcic pneumonia. With a single exception the results were striking, and in 1 instance they were remarkable. This case should be related because it provides a clear instance (the first to be observed by us) in which a specific effect of penicillin on the disease could be noted.

A 1 year old child presented the clinical and roentgenologic evidence of an empyema complicating pneumonia. Aspiration revealed pus, out of which was grown Staph. aureus in pure culture. At operation empyema was not encountered; instead there were two small collections of pus in the lung. As the roentgenologic and clinical evidence of empyema persisted, another operation was undertaken on the assumption that empyema had been overlooked. This operation revealed widespread pulmonary suppuration, obviously not amenable to surgical drainage. Improvement was rapid and decisive following therapy with penicillin, with surprisingly early and complete (roentgenologic) clearing up of the pulmonary lesion.

Bennett and Parkes [30] and Blake and Craige [31] have reported instances in which penicillin appeared to be of definite value in staphylococcic pneumonia. Our experience with penicillin therapy is too limited to warrant any broad statement; yet it appears quite safe to say that staphylococcic pneumonia can no longer be regarded as a self-limited disease slightly if at all affected by drugs.

We believe that pulmonary infections in very young infants are often of staphylococcic origin and, therefore, that penicillin therapy is

30. Bennett, T. I., and Parkes, T.: Lancet **1**:305, 1944.

31. Blake, F. G., and Craige, B., Jr.: Yale J. Biol. & Med. **15**:507, 1943.

imperative for all young infants suffering from pneumonia as soon as they come under observation, in the expectation that cure will be often achieved in a disease which in certain varieties has been characterized by an excessively high mortality.

Surgical.—Surgical intervention directed against the pleural complication of staphylococcic pneumonia can be life saving in the acute stage. In this connection there are two important facts to be emphasized: first, that pleural complications are common and can prove fatal in a short time if uncared for; second, that pleural complications may occur abruptly and unexpectedly at an early stage of the pulmonary infection. As already noted, patients will not recover solely because of timely and adequate treatment of the pleural infection. In some of our cases the suppurative lesion in the lung was so severe and extensive (as ascertained at autopsy) that a significant result by drainage of the pleural infection could not be anticipated. Nevertheless, drainage should be instituted regardless of the known or assumed severity of the pulmonary lesion, because operative recoveries which were not anticipated have been seen. The unequivocal diagnosis of bronchopneumonia due to the staphylococcus can at best only be suspected on roentgenographic examination in most instances. In the case of an infant or a young child, one may assume that a perforative pulmonary lesion is due to a staphylococcic infection. However, an infection due to the streptococcus or the pneumococcus, which produces the same or a similar pleuropulmonary lesion, requires identical surgical treatment, and the identification of the infecting organism therefore is not of clinical moment except as it concerns the addition of penicillin to surgery.

Although open pleural drainage has been advocated by some writers, we believe that closed drainage should comprise the sole primary treatment of a rapid accumulation of pus and air, or of pus alone, in the free pleural space. It is the best means of influencing decisively not only the displacement of the heart and mediastinum but also the acute infection in the pleural space. The consistency of the pus within the pleura, thick or thin, is of no import. Concerning treatment by aspiration, we know of more than 1 instance in which death has followed temporization with Potain aspirations, which were employed because the infection in the lung was regarded as too acute or the child too ill for closed drainage to be instituted. We believe that the arguments advanced elsewhere [32] in favor of closed drainage as against repeated aspiration apply with particular force to staphylococcic pleuritis. We perceive many advantages in the pleural administration of penicillin by the closed drainage system but oppose temporization with aspiration

32. Neuhof, H., and Hirshfeld, S.: Suppurative Pleuritis in Children, Am. J. Dis. Child. **44**:973 (Nov.) 1932.

and administration of penicillin in acute tension empyema or pyopneumothorax when surgical drainage is indicated. We have seen only unfortunate sequelae to such temporization and have yet to see a cure.

Closed drainage alone may prove to be curative, particularly in conjunction with penicillin. In most instances, however, subsequent open drainage, performed when the child's general condition is satisfactory, will be necessary. At such operations, drainage should be instituted at the site of the bronchial fistula which often is present, and healing will usually occur. However, pulmonary cavitation and bronchial fistulas may persist if the destructive pulmonary lesion is extensive. Under the latter circumstances the simple expedient of fat graft [33] will usually lead to cure. In rare instances it has been necessary to attempt to plug a large perforated pulmonary lesion by a fat graft during the acute stage. These were cases in which dangerously large quantities of air escaping through the closed drainage system jeopardized the life of the child.

A primary open operation is indicated for the drainage of a well encapsulated empyema or pyopneumothorax even in a young child or an infant. Experience has shown that closed drainage in such cases is inadequate, invites multilocularity and must be followed by open drainage. Little is gained by deferring definitive drainage. The unnecessary prolongation of a toxic state and the needless difficulties frequently encountered in delayed open operations are arguments against primary closed drainage in infants or children suffering from encapsulated pleural infections.

Foci of suppuration in the midst of pneumonic infiltration are features of staphylococcic pneumonia and as such are not of surgical significance. If despite penicillin therapy a true pulmonary abscess is formed, it is a circumscribed lesion usually of substantial proportions and is identified by its roentgenographic features. Recovery may follow the spontaneous evacuation of the abscess via the bronchial tree. A pulmonary abscess should be surgically treated in order to (1) achieve cure safely, (2) obviate perforation into the pleural space, (3) prevent spread of the infection within the lung and (4) exclude the likelihood of a chronic abscess, to whose insidious evolution reference has been made. Since the abscess is situated superficially within a pulmonary segment and is overlaid by agglutinating visceroparietal pleural adhesions, a one stage operation through pleural adhesions usually can be safely performed. The abscess must be carefully localized by roentgenograms immediately before operation, with the addition of the spot localization method of Rabin [34] whenever there is any doubt as to its precise situation. In the rare instances in which the abscess faces a fissure, a special

33. Neuhof, H.: J. Thoracic Surg. **7**:23, 1937.
34. Rabin, C. B.: J. Thoracic Surg. **10**:662, 1941.

technic is required in order to avoid infecting the general pleural space. Recovery and cure followed drainage of the pulmonary abscess in our 3 cases of staphylococcic pulmonary abscess, as in all our cases of aerobic abscess of the lung reported elsewhere.[26]

REPORT OF CASES

Data in all the cases on which this study is based are tabulated at the end of the paper, but a number of instances have been selected and are detailed herewith in order to illustrate particular features of the disease.

The following case is an example of the acute disseminated form in which there is little or no pleural involvement and which is not epidemic in character.

CASE 1.—F. V., a 3 week old girl, was admitted to the pediatric service on June 21, 1935, with a history of a mild infection of the upper respiratory tract five days prior to admission. On June 19 the parents noted that the infant was breathing rapidly, and the following day the temperature was found to be 102 F. A moderate cough was present. On admission the infant appeared acutely ill and toxic. There was dyspnea, but no cyanosis. Examination of the chest revealed impaired resonance, diminished breath sounds and crepitant rales over the lower lobe of the right lung. The abdomen was prominently distended. While under observation, the child's temperature ranged between 103 and 104 F. A 40 cc. blood transfusion was given, and oxygen therapy was started. However, the illness progressed, and the infant died on June 22. Roentgenographic examination of the chest on June 21 revealed evidence of consolidation in the lower lobe of the right lung. The hemoglobin content was 72 per cent; the red blood cells numbered 4,700,000 and the white cells 7,500, with 24 polymorphonuclear leukocytes, 62 lymphocytes and 14 mononuclears. At postmortem examination the abdomen was observed to be greatly distended. There was no free fluid in the peritoneal cavity. On examination of the thorax, fibrinopurulent, friable adhesions were found binding the visceral to the parietal pleura on the right side over the lower lobe. There were a few drops of red-tinged purulent exudate. The lower lobe of the right lung was voluminous, noncrepitant and firm, while in places it was broken down and cystic in consistency. Its surface was dark blue and hemorrhagic in appearance, with paler violet areas. There were millimeter-sized purulent foci as well as small, broken-down, dirty brown areas, which could be probed for about 1 cm. within the lung, revealing communications between the parenchyma and the pleural cavity. The cut surfaces showed a similar appearance. The bronchi in the lower lobe contained pus within their lumens. Culture revealed a pure growth of Staph. aureus.

In the following case of acute disseminated pneumonia, the gastrointestinal completely overshadowed the pulmonary symptoms.

CASE 5.—M. A. W., a 4 month old girl, was admitted to the hospital on Oct. 28, 1934 for the regulation of feeding. This infant had been vomiting occasionally since earliest infancy and had not been gaining in weight satisfactorily. She was afebrile, and the blood count was normal. On the sixth hospital day (November 2) the temperature suddenly rose to 103 F., the throat was found to be moderately injected and a mild catarrhal otitis media on the left side was

noted. Results of examination of the chest were negative. The temperature remained elevated, but the infant's general condition appeared satisfactory. Abdominal distention gradually became more prominent. On November 4 at about 6:30 a. m. the child suddenly became dyspneic and intensely cyanotic. The pulse was rapid, weak and thready. Because of vomiting, occasional diarrhea and severe abdominal distention, it was felt that the clinical picture was referable to alimentary intoxication. The child was treated with a continuous infusion of 5 per cent dextrose in isotonic solution of three chlorides and was placed in an oxygen chamber. At first oxygen relieved the cyanosis and dyspnea, but both soon became intense again. Abdominal distention was tremendous, and numerous unsuccessful attempts were made to relieve this distressing symptom. The temperature ranged between 101 and 105 F. Late in the course of the illness, dulness was noted over the bases of both lungs and in both axillas, but this was interpreted as being secondary to abdominal distention and the resultant elevation of the diaphragm. The course of the disease was rapidly progressive, and death occurred on November 7. At the postmortem examination loops of intestine were observed to be distended, but there was no other pathologic condition within the abdominal cavity. A staphylococcic bronchopneumonic infiltration of the upper lobe of the left lung, with abscess formation, was present. The pleural cavities were uninvolved.

The following case was of the epidemic type of the acute disseminated form with minimal pleural involvement.

CASE 7.—W. Y., a 10 year old boy, was admitted to the hospital on Nov. 9, 1934, with a history of having been well until that morning. He awoke at 6 a. m. complaining of a sore throat, and his temperature was found to be 104.6 F. At 10 a. m. he complained of pain in the right axilla, and it was noted that his respirations were somewhat labored and that he was hoarse. At that time his temperature was 105 F. The boy was admitted to Mount Sinai Hospital at 2 p. m. with a temperature of 106.8 F. He was acutely and severely ill and appeared toxic and in respiratory distress. The respirations were rapid, and an inspiratory crow was present. There was a dusky cyanosis. Examination of the chest revealed dulness on percussion anteriorly and in the right axilla. The auscultatory findings consisted of distant breath sounds over the area of dulness. The diagnosis on admission was acute laryngotracheobronchitis and bronchopneumonia. A roentgenogram of the chest revealed an area of consolidation on the right side from the second rib to the diaphragm. The hemoglobin content was 83 per cent; the red cells numbered 5,100,000 and the white cells 3,700, with 54 per cent polymorphonuclear leukocytes. A culture of material from the throat grew Staph. albus, Streptococcus viridans and Pneumococcus, type IV.

Laryngologic consultation was obtained because of the stridor. The airway was found to be adequate, and no exudate was found. The child was placed in an oxygen tent, and stimulants were administered. The course was rapidly downhill, and death occurred at 11:30 p. m. on the day of admission, less than twenty-four hours after the onset of the disease. Postmortem examination revealed necrotizing tracheitis and influenzal bronchopneumonia complicated by multiple pulmonary staphylococcic abscesses.

The following case is an example of the acute disseminated form of the disease with diffuse pyopneumothorax. Rapid improvement fol-

lowed drainage of the pleural infection, but it did not influence the course of the pulmonary disease.

CASE 9.—B. W., a 3 year old girl, was seen on Nov. 24, 1935. She had a history of a slight fever, cough and malaise for three weeks. This condition was followed by an increasing cough and fever, and on November 17 a diagnosis of pneumonia was made. On November 23 there developed acute dyspnea and progressively severe cyanosis. The following day the patient was admitted to the hospital. On examination the child was observed to be acutely ill and appeared to be in shock. Respirations were rapid and labored. There were decided dyspnea and intense cyanosis. The mediastinum was shifted to the left. There were dulness and absence of breath sounds over the lower right side of the chest, and a loud metallic tinkle could be heard in this area. The pulse rate was 160 per minute. The temperature was 100.4 F. The clinical impression was of ruptured pulmonary abscess, with diffuse pyopneumothorax and displacement of the mediastinum. This impression was confirmed by roentgenographic examination which demonstrated a large pneumothorax with relatively little fluid. The hemoglobin content was 80 per cent; the red blood cells numbered 4,460,000 and the white cells 23,600, with 85 per cent polymorphonuclear leukocytes. Aspiration was performed on the right side of the chest, and only air under pressure was obtained. An emergency stab thoracotomy was then done, which resulted in a gush of air escaping through the under-water drainage system, followed by an escape of grayish pus. There was a critical response to the relief of pleural pressure. The child appeared comfortable, and the cyanosis and dyspnea disappeared. On the evening of November 25 there was noted the sudden expulsion of a mucopurulent plug from the drainage tube followed by a gush of air for several minutes. It was felt that this probably represented rupture into the pleural cavity of another pulmonary abscess. Following this, extremely large amounts of air were seen to be bubbling through the drainage system and the child's general condition became worse. Large quantities of air escaped through the closed drainage system. Death occurred on November 28. Postmortem examination revealed a purulent bronchitis; suppurative staphylococcic bronchopneumonic involvement of the upper, middle and lower lobes of the right lung; a perforated pulmonary abscess in the upper lobe with secondary pyopneumothorax, and acute fibrinous pericarditis with effusion.

The following case is another illustration of the acute disseminated form of the disease with diffuse pyopneumothorax. Here relief of the mediastinal displacement prevented early death. The underlying pulmonary disease subsided, and the patient recovered.

CASE 14.—G. R., a 2½ year old boy, was admitted to the hospital on Nov. 17, 1933, with a history of a mild infection of the upper respiratory tract nine days before admission. He was soon well from this infection and was allowed to be up and out-of-doors. On November 11 the temperature suddenly rose to 105 F., and the child appeared to have pain in the chest. The temperature fluctuated between 102 and 105 F. for the next few days. During this time there were cough and some dyspnea. About twenty-four hours before admission the child became more seriously ill. Dyspnea was more pronounced, and at times he was delirious. At the time of his admission he was acutely ill, toxic and deeply cyanotic. The abdomen was distended, tense and tender to palpation. The right side of the chest was dull to flat on percussion, and the breath sounds

were distant over this area. The heart was displaced to the left, its left border being 3 cm. outside the left nipple line. The urine was normal. The hemoglobin content was 78 per cent; the red cells numbered 4,920,000 and the white cells 12,300, with 63 per cent polymorphonuclear leukocytes. A roentgenographic examination of the chest revealed evidence of pyopneumothorax, with displacement of the heart and the mediastinum. Two hundred and fifty cubic centimeters of thin yellow odorless pus was aspirated from the chest. On culture this was proved to contain a pure growth of Staph. aureus. Despite oxygen therapy the child's general condition grew rapidly worse. The temperature remained high. An indurated area developed about the site of the thoracic puncture. On November 20 the child was in critical condition. Dyspnea was pronounced. In view of the fact that the pyopneumothorax had been demonstrated prior to therapeutic aspiration, it was felt that the patient had a staphylococcic abscess of the lung with perforation into the pleura. An emergency closed drainage was performed for relief of mediastinal embarrassment. The child was kept in an oxygen tent, and transfusions were given. About nine or ten days after the operation the child seemed decidedly better. However, he continued to run a febrile course. On December 20 a roentgenogram of the chest showed on the lateral view a collection of fluid just above the diaphragm. A rib resection was performed on December 22, and the cavity was packed. The temperature gradually dropped to normal. Convalescence was slow. We have had an opportunity to follow this patient for twelve years, and he has remained in good health. A recent roentgenogram of the chest was normal.

The next case is an example of the acute circumscribed form of the disease in which the pathologic condition remained localized within the lung (pulmonary abscess). This abscess was drained surgically before rupture into the pleural cavity. Therapy with sulfonamide compounds was started early, but the pulmonary process progressed.

Case 21.—R. R., a 2½ year old girl, was admitted to the hospital on April 4, 1941. On April 12 she had a mild bronchitis, but she did not appear ill. On April 16 the temperature was 104 F., and evidence of pneumonia was found at the base of the right lung. Sulfapyridine, 2 Gm. daily, was given, without any appreciable effect. On the third day the same dose of sulfathiazole was started and continued until April 22. Because of the failure to respond to sulfonamide therapy, the patient was hospitalized at another institution. Two cultures of material from the throat contained a pure growth of Staph. aureus. Roentgenograms of the chest revealed an area of density in the upper two thirds of the right lung, in the midst of which were seen two areas of increased illumination about the size of a quarter. No fluid level could be demonstrated. The temperature remained elevated, and on April 27 the patient was admitted to the Mount Sinai Hospital. The roentgenograms revealed the features of an abscess facing the long fissure. Open operation was performed. A large pulmonary abscess was found. Its roof consisted of a thin layer of compressed avascular pulmonary tissue. The cavity was opened, and air and thick pus under tension escaped. The cavity was smooth lined and multilocular and presented the orifices of several bronchial fistulas. Following surgical drainage the temperature dropped to normal. Convalescence was rapid. The child was discharged from the hospital on May 8. She has remained well, and a recent roentgenogram of the chest reveals no abnormalities.

There now follows an example of the acute circumscribed type of staphylococcic pneumonia with an encapsulated pyopneumothorax. This

child also presented confusing gastrointestinal symptoms, making difficult the differentiation of the lesion from an acute surgical abdominal lesion.

CASE 33.—J. W., a 6 year old boy, was admitted to the hospital on Jan. 26, 1939, with a history of having had a mild cough for three days. During this time he was afebrile. On the morning of admission he awoke with pain in the right lower quadrant of the abdomen. His temperature was normal. At noon he vomited; the temperature at this time was 103 F. At 2 p. m. it had risen to 104 F. The child was admitted at 5 p. m., appearing very ill. There was some dyspnea, and there was impaired resonance over the lower lobe of the right lung. The abdomen was distended and rigid throughout, and there was generalized abdominal tenderness, most pronounced in the right lower quadrant. A roentgenogram of the chest showed exaggerated markings at the base of the right lung, but this was insufficient to establish a diagnosis of pneumonia. An abdominal puncture was performed first in the left lower quadrant and then in the right lower quadrant. No fluid was obtained. The hemoglobin content was 12.4 Gm.; the red cells numbered 4,100,000 and the white cells 15,350, with 89 per cent polymorphonuclear leukocytes. Sulfapyridine was given by mouth in a dose of 1 Gm. six times a day. While the patient was under observation, evidence of pulmonary consolidation became manifest. Roentgenographic examination on January 27 confirmed this clinical finding. Dyspnea gradually became more intense; on January 28 cyanosis became apparent and oxygen was given in addition to the sulfonamide compounds. Several blood transfusions were also administered. On February 3 the child appeared in a critical condition. Dyspnea was more pronounced. Cyanosis was present despite oxygen therapy. The right side of the chest was dull posteriorly and over the lower half of the right axilla. Over this area the breath sounds were absent. There were no rales or evidence of mediastinal displacement. The abdomen was distended and tender to palpation. A roentgenogram revealed a dense shadow in the lower half of the chest on the right side, within which was seen a large loculated cavity with a fluid level at the tenth rib posteriorly. A nonodorous thick green pus was aspirated from the chest. Closed under-water drainage was promptly instituted. Rapid clinical improvement was noted after surgical drainage, but the temperature remained elevated. On February 14 a rib resection was done, and a large cavity with numerous bronchial fistulas was found. Convalescence was rapid and uneventful following this procedure. On March 22 iodized oil was introduced into the sinus tract in the lower lobe of the right lung. The oil was seen to enter the bronchus of the posterolateral division of this lobe immediately, and then it outlined all the bronchi of the right lung. Cultures of blood taken on January 26 and February 4 were negative. A culture of sputum on January 26 grew Str. viridans and Micrococcus catarrhalis. On January 31 a laryngeal swab was cultured and reported as containing Str. viridans and Staph. aureus A. Frequent blood counts were done, the white blood cell counts varying between 16,350 and 75,000 per cubic millimeter. Doses of 6.0 Gm. daily of sulfapyridine were given from January 26 to February 5, without any appreciable effect. The follow-up was satisfactory. Two years after discharge the boy was in excellent health. A roentgenogram of the chest was normal.

The following case is an example of staphylococcic pneumonia apparently complicating a virus disease. The pulmonary condition was inadequately treated surgically, with a resultant chronic course. Cure followed adequate drainage of the pulmonary abscess eight months later.

CASE 40.—L. A., a 6 year old boy, was admitted to Mount Sinai Hospital Oct. 18, 1928. In April the patient contracted measles. While he was still ill from this disease, it was noted that the temperature gradually rose, and evidence of pulmonary consolidation was found. After an illness of about seven days, a diagnosis of empyema was made, and the child was taken to a hospital for surgical care. A thoracotomy and drainage of an empyema were performed, and the patient was returned home three and one-half weeks later. He seemed well for about a month and then was noted to have a return of fever. There was no dyspnea. Following this episode recurrent febrile periods were observed. A cough gradually became apparent. The patient was admitted to Mount Sinai Hospital because of cough, fever, anorexia and loss of weight. Roentgenographic examination demonstrated a pleural effusion at the base of the right lung, extending upward to the fifth rib in the axillary line. The hemoglobin content was 58 per cent; the white blood cells numbered 13,700 per cubic millimeter, with 68 per cent polymorphonuclear leukocytes. The child did not appear acutely ill. On October 23 a roentgenogram showed an encapsulated collection of fluid in the right side of the chest, which had increased in size. On aspiration a thick green pus was obtained. A thoracotomy was then done, and 150 cc. of pus was removed. This fluid was cultured, and a pure strain of Staph. aureus was grown. Convalescence was normal. Iodized poppyseed oil 40 per cent was injected into the sinus and revealed a narrow tract leading from the chest wall at about the level of the seventh interspace into the pleural cavity, in which there was an irregular triangular pocket extending from the seventh interspace to the ninth rib. The upper part of the pocket was not outlined. The child was discharged on November 22. Shortly after he arrived home, his temperature rose to 103 F. and persisted at this level. He was readmitted on November 30. The hemoglobin content was 64 per cent and the white cell count 34,400, with 83 per cent polymorphonuclear leukocytes. From November 30 to December 6 the temperature had a daily fluctuation between 100 and 103 F. A roentgenogram showed again an enlargement of the pleural effusion previously noted. On December 7 a thoracotomy was performed. A large collection of pus was found. This was sharply localized in an empyema cavity which extended upward from the midchest with a narrow prolongation anteriorly and superiorly to or near the apex. A posterior recess led directly into a small collection of pus within necrotic lung. This was interpreted as being the original pulmonary focus. Two overlying ribs were resected, and the pulmonary and pleural lesions were widely drained. Postoperatively, a blowing bronchial fistula was noted. The temperature dropped to normal shortly after operation and remained so thereafter. The fistula closed, and the boy was discharged on Feb. 6, 1929. He was followed for three years and remained in excellent health. A roentgenologic check-up revealed no residue of pulmonary infiltration.

The following case is one of pulmonary cavitation associated with a large sympathetic pleural effusion from which Staph. albus A was isolated. Recovery was possibly aided by sulfathiazole.

CASE 31.—V. A., a 15 month old girl, became ill on Feb. 1, 1942, with a cough, nasal discharge and fever. She was then well until Feb. 4, when her temperature rose to 105 F. At that time abdominal pain and prominent abdominal distention were noted. The child's physician found signs of pneumonia and referred the patient to the hospital on February 7, at which time she was acutely ill. Evidence of pulmonary consolidation was found at the base of the left lung. The white blood cell count was 12,850 per cubic millimeter, with 78 per cent poly-

morphonuclear leukocytes. The child was given sulfathiazole by mouth (0.2 Gm. per kilogram of body weight). Her temperature remained elevated, ranging from 101 to 104 F. Material cultured from the nares on two occasions grew a pure strain of Staph. albus A, while cultures of material from the throat contained this organism in addition to Str. viridans A and beta hemolytic streptococci. A roentgenogram of the chest showed evidence of a pneumonic infiltration of the lower lobe of the left lung, with some fluid in the left pleural cavity. On February 13 dyspnea was more severe. The entire left side of the chest was dull to percussion, and the breath sounds were distant or absent. A culture of blood was sterile. On February 14 a roentgenogram showed a large pleural effusion in the axillary portion of the left side of the chest from the diaphragm well up toward the apex. In addition there was a cavity with a fluid level in the left lower pulmonary field 1¼ inches (3.2 cm.) in length. This was situated adjacent to the interlobar fissure. Eighty cubic centimeters of clear fluid was aspirated from the pleural cavity. This contained Staph. albus A on culture. At this time administration of sulfathiazole was discontinued. In the presence of pulmonary cavitation, it was feared that chemotherapy might mask some of the symptoms, making it impossible to evaluate properly the operative indications. Several transfusions of blood were given. The temperature gradually fell to normal levels, and the child's general condition appeared good. Daily roentgenograms of the chest showed no alteration in the size or shape of the cavity, which contained a fluid level. On February 19 the temperature rose to 102 F., and there was evidence of acute otitis media. Administration of sulfathiazole was again started to combat the otitic infection. The temperature promptly dropped to normal, and the drug was continued until February 23, at which time a generalized morbilliform eruption was noted. At this time the administration of sulfathiazole was discontinued. A roentgenogram showed a considerable decrease in the amount of fluid in the left pleural cavity and some reduction in size of the pulmonary cavity. The child remained afebrile, and clinical improvement was progressive. On March 3 the roentgenogram showed a distinct reduction in size of the area of rarefaction, and on March 11 the area of rarefaction had disappeared. The child was discharged on March 13, has since been seen for a follow-up and has been found in excellent health. During the period of observation from Feb. 8, 1942 to February 20, the white blood cell counts ranged from 12,850 to 24,800 per cubic millimeter. On February 23 the count was 8,300 per cubic millimeter, and it subsequently remained within normal limits.

SUMMARY

Pneumonia due to the staphylococcus and occurring in infancy and childhood is of the suppurative variety. Proved cases are reported infrequently, but the disease probably is far from rare.

The description of the clinical entity given here is based on the study of more than 40 proved cases. A concept of the pathogenesis of the disease and its classification into a number of types are proposed. The pathologic and clinical manifestations of the various types, with illustrative case reports are described. Emphasis is placed on certain roentgenographic features which when present are deemed to be characteristic or at times pathognomonic, of the disease.

Until the advent of penicillin, staphylococcic pneumonia, often characterized by high mortality, was in the group of self-limited dis-

Case	Age, Sex	Clinical Manifestations	Roentgenographic Features	Pathologic Observations at Operation	Broncho-pleural Fistula	Result
			1. Acute Diffuse Suppuration: A. Little or No Pleural Involvement			
			(1) Nonepidemic Type			
1	3 wk. F	Severe pneumonia, marked abdominal distention and stormy, fatal course	Consolidation of right lower lobe	.....	Yes, at autopsy	Died in 3 days. Autopsy: diffuse hemorrhagic consolidation right lower lobe; multiple pulmonary abscesses with bronchopleural fistula and interlobar empyema
2	7 wk. M	Severe diarrhea for 10 days, followed by sudden onset of pulmonary symptoms; rapidly fatal	Collapse of left lower lobe with irregular areas of rarefaction	.....	No	Died in 2 days. Autopsy: diffuse hemorrhagic consolidation of left lower lobe, multiple small abscesses clustered about bronchioles; pleurae normal
3	14 mo. F	Pneumonia treated with chemotherapy; marked abdominal distention; died 12 hr. after admission to hospital	Dense infiltration entire right lung; small areas of rarefaction lower half of right lung; empyema (right); infiltration left upper lobe	.....	Yes, at autopsy	Died 8 days after onset. Autopsy: confluent bronchopneumonia of right lower, right upper and left lower lobes, with multiple pulmonary abscesses; localized pyopneumothorax (right)
4	9 days F	Epidemic diarrhea of newborn; gastrointestinal symptom complex masked pulmonary disease throughout; died 6 hr. after admission	.....	.....	No	Died 4 days after onset of diarrhea. Autopsy: confluent bronchopneumonia of all lobes with multiple abscesses; fibrinous pleuritis
5	4 mo. F	Patient admitted for prolonged vomiting and failure to gain; on sixth hospital day fever developed with tremendous abdominal distention; gastrointestinal syndrome masked pulmonary symptoms	.....	.....	Yes, at autopsy	Died 5 days after admission. Autopsy: diffuse bronchopneumonia of left lung, with scattered areas of hemorrhage and necrosis—multiple small abscesses with one large confluent abscess; bronchopleural fistula and pyopneumothorax on left
6	11 wk. M	Pneumonia followed by pleural effusion; severe cyanosis and tachypnea	Large pleural effusion	Few flakes of thick pus seen, followed by sudden rupture of abscess into pleura	Yes	Rapid downhill course; died 2 days after admission. Autopsy: (1) acute purulent tracheobronchitis; (2) suppurative bronchopneumonia, lower left lobe, multiple abscesses; (3) empyema, left side; (4) acute fibrinopurulent pericarditis
			(2) Epidemic Type			
7	10 yr. M	Severe acute laryngotracheobronchitis; rapidly fatal	Consolidation of right side of chest from second rib to diaphragm	.....	No	Died within 24 hours. Autopsy: necrotizing tracheobronchitis; bilateral diffuse bronchopneumonia with considerable hemorrhage; multiple abscess right lower lobe; fibrinous bilateral pleural exudate

8	10 yr. M	Severe, rapidly fatal pneumonia complicated by tracheitis	Irregular infiltration of entire right lung	.....	..	Died within 48 hours of admission; necrotizing tracheitis and bronchitis; confluent bronchopneumonia, right upper, middle lobes, left lower lobe with bilateral multiple abscesses
			B. Widespread Pleural Involvement			
9	3 yr. F	Infection upper part of respiratory tract followed by pneumonia, dyspnea and cyanosis; trachea shifted; metallic tinkle heard	Large pyopneumothorax with fluid level	Pus and air under tension	Yes	Died 4 days after closed drainage. Autopsy: (1) purulent bronchitis; (2) suppurative diffuse bronchopneumonia; (3) ruptured pulmonary abscess (right upper lobe); (4) acute pericarditis
10	1 mo. M	Onset of dyspnea a few hours before admission; persistent severe abdominal distention	Consolidation of right upper lobe; pleural effusion	Empyema	No	Died 7 hours after closed drainage. Autopsy: (1) suppurative bronchopneumonia, right upper, middle and lower lobes and left lower lobe, with abscess formation in right lower lobe; (2) empyema (right)
11	2 yr. F	Pneumonia 14 days before admission; pyopneumothorax on admission	Pyopneumothorax (left)	Air and pus in pleura	Yes	Died 24 hours after closed drainage. Autopsy: (1) diffuse bronchopneumonia; (2) abscess left upper lobe with bronchopleural fistula and (3) pyopneumothorax (left)
12	4 yr. F	Pneumonia left lower and upper lobes; severe abdominal distention	Pyopneumothorax (left)	Empyema	Yes	Died few hours after closed drainage. Autopsy: (1) purulent bronchitis; (2) pyopneumothorax (left); (3) diffuse bronchopneumonia; (4) acute fibrinous pericarditis
13	18 mo. M	Pneumonia and empyema complicating measles; marked abdominal distention	Pleural effusion (right)	Empyema	Yes	Did well after closed drainage; 8th day, sudden dyspnea, rise of temperature and death. Autopsy: (1) diffuse pneumonia; (2) pyopneumothorax (right); (3) multiple pulmonary abscesses right lower lobe and (4) fibrinopurulent pericarditis
14	2½ yr. M	Pneumonia followed by sudden onset of dyspnea; marked abdominal distention	Pyopneumothorax with shift of mediastinum	Empyema	Yes	Stab thoracotomy; stormy postoperative course with gradual improvement; secondary rib resection; follow-up for 12 years; roentgenogram of chest normal
15	3 yr. M	Pneumonia followed by pleural effusion; cellulitis of chest wall following aspiration	Pleural effusion (left)	Empyema	No	Closed drainage; stormy postoperative course; prolonged convalescence; follow-up for 3 years; roentgenogram normal

Analysis of Cases of Staphylococcic Suppurative Pneumonia—Continued

Case	Age, Sex	Clinical Manifestations	Roentgenographic Features	Pathologic Observations at Operation	Broncho-pleural Fistula	Result
16	6 wk. M	Pneumonia followed by empyema; furuncles of chest wall after aspiration; prominent abdominal distention	Pulmonary infiltration of right side of chest with small areas of rarefaction and widespread pleural involvement	Empyema	Yes	Closed drainage with rapid recovery; 3 mo. later sepsis (Pneumococcus type XXI) and meningitis; death. Autopsy: (1) suppurative bronchopneumonia with abscess formation; (2) pyopneumothorax (right) (Staph. aureus); (3) acute suppurative meningitis (Pneumococcus type XXI; (4) sepsis (Pneumococcus type XXI)
17	3 yr. M	Pneumonia followed by pleural effusion; bulging chest wall (abdominal distention with questionable peritonitis)	Pneumothorax (right)	.....	Yes	Closed drainage with stormy postoperative course; secondary thoracotomy with rib resection; uneventful convalescence; patient readmitted 2 wk. after discharge for secondary pleural drainage; numerous adhesions; 1 year follow-up; roentgenogram normal
18	2 yr. F	Pneumonia followed by pleural effusion; phlegmon of chest wall; pronounced abdominal distention	Consolidation left upper lobe; pleural effusion (left) with shift of mediastinum	.....	Yes	Closed drainage with prolonged convalescence; 3 year follow-up; child well
19	10 wk. M	Diffuse pneumonia with noticeable respiratory difficulty and pronounced abdominal distention (peritonitis ?)	.....	.....	..	Attempt to treat with multiple aspirations; downhill course; closed drainage February 19 with death 30 hours later; no postmortem examination
			II. Acute Localized Suppuration			
20	2 yr. F	Pneumonia treated with sulfapyridine for 7 days prior to admission	Pulmonary abscess apical portion of right lower lobe, adjacent to long fissure	Abscess in right lower lobe, with beginning appearance of lattice lung; many bronchial fistulas	No	Positive blood culture on admission; several cultures negative thereafter; convalescence complicated by appearance of numerous furuncles; follow-up for 1 year; child well
21	2½ yr. F	Twelve days before admission pneumonia treated with sulfapyridine and then with sulfathiazole	Consolidation of right upper lobe; areas of rarefaction	Pulmonary cavity with air and thick pus under pressure; cavity smooth, lined and multilocular; several bronchial fistulas	Yes	Rapid drop in temperature with uneventful convalescence

22	18 mo. M	Onset with convulsions and paresis of right upper and lower extremities; diagnosis of encephalitis; on eleventh day onset of cough and fever and pulmonary infiltration; pleural effusion	Pleural effusion; pulmonary abscesses	Encapsulated pleural effusion (sterile), sympathetic effusion; abscss of right middle lobe with freely blowing bronchial fistula	Yes	Stormy postoperative course with gradual improvement; when seen 2 yr. later, chest normal; postencephalitic syndrome
23	9½ yr. F	Onset with epidemic grip, many contacts; illness followed by fever, cough, pain in chest; treated with sulfanilamide and sulfathiazole, without apparent result	Encapsulated pleural effusion (left)	Encapsulated empyema in subscapular and apical area, containing debris and thin pus	Yes	Rapid cure following surgical drainage
24	5½ yr. F	Onset with acute purulent otitis media, followed by pulmonary consolidation	May 13: large pleural effusion (right); May 19: pneumonic area in right lung with cavity in upper portion; May 23: partial pneumothorax (right), numerous small cavities	May 13: closed drainage, considerable pus and air escaped; May 29: open drainage, many pulmonary cavities noted	Yes	Large amount of pulmonary slough; interstitial pneumonitis; recovery after fat graft
25	2 mo. M	Cough and fever	Large pleural effusion on right with partial pneumothorax	Closed drainage	Yes	Uneventful recovery
26	3½ yr. F	Pneumonia followed by febrile course	Pleural effusion (right)	Open operation	Yes	Uneventful recovery
27	10 yr. M	Abdominal pain right lower quadrant; fever, convulsions, delirium and acidosis	Confluent bronchopneumonia; pleural effusion (small)	Open operation, cavity with bronchial fistula	Yes	Rapid recovery; 1 year follow-up
28	12½ yr. F	Pneumonia followed by pain in chest and prolonged fever	Pleural effusion	Empyema and bronchial fistula	Yes	Gradual improvement complicated by cellulitis about wound
29	2½ yr. M	Chill, cough and abdominal pain; bronchopneumonia and empyema; pure culture Staph. albus obtained 4 times	Pleural effusion	Empyema	No	Gradual recovery
30	5 yr. M	Otitis media; pneumonia; empyema—Staph. albus	Pleural effusion	Very large empyema cavity anteriorly with a second area separated by ridge of lung	No	Complicated by purulent otitis media—prolonged febrile period; secondary drainage of empyema; follow-up 7 yr.; child well
31	15 mo. F	Abdominal pain, fever, pneumonia, pleural effusion—Staph. albus; treated with sulfathiazole	Feb. 9: pneumonic infiltration with some pleural exudate; Feb. 14: large effusion with pulmonary cavitation	.....	No	Cure without surgical intervention
32	10½ mo. M	Otitis media, pneumonia, empyema; treated with sulfathiazole from onset	Pleural effusion; encapsulated	Closed drainage on two occasions	Yes	Improvement followed second operation; child well when seen on long follow-up
33	6 yr. M	Abdominal pain in right lower quadrant; rigidity and fever; appendicitis or peritonitis considered; pneumonia, empyema; treated with sulfapyridine early and adequately	Jan. 26: exaggerated markings right base; Jan. 27: consolidated right lower lobe; Feb. 3: multilocular pulmonary shadows	Large pulmonary cavity with many bronchial fistulas	Yes	Improvement followed closed drainage; later open drainage with rapid cure; 2 yr. follow-up; roentgenogram normal

Analysis of Cases of Staphylococcic Suppurative Pneumonia—Continued

Case	Age, Sex	Clinical Manifestations	Roentgenographic Features	Pathologic Observations at Operation	Broncho-pleural Fistula	Result
34	1 mo. F	Pneumonia with marked abdominal distention; treated with sulfapyridine early; empyema	Dec. 2: consolidation; Dec. 4: pleural exudate	Pulmonary cavity pointing toward fissure	Yes	Recovery; follow-up for 6 mo.; child well
35	6 yr. M	Chickenpox and bronchitis followed by pneumonia and empyema; chronic course; Staph. albus	Encepsulated effusion (left)	Large collection of pus	Yes	Good recovery after surgical drainage; 1½ yr. follow-up; child well
36	5½ yr. M	Grip followed by severe pain in chest, pneumonia and chronic empyema	Encapsulated pleural effusion (right)	Large encapsulated empyema with perforation of lung	Yes	Uneventful, slow recovery
			III. Subacute and Chronic Suppuration			
37	7 yr. M	Fever, cough, pain in chest, large pleural effusion (sympathetic, simulating tuberculous effusion) and chronic course prior to surgical drainage	Very large pleural effusion	Clear loculated sympathetic effusion adjacent to empyema cavity containing large fibrinopurulent exudate	No	Rapid recovery; 3 yr. follow-up
38	7 yr. M	Pneumonia followed by chronic empyema	Large pleural effusion (left)	Empyema containing 96 ounces (2,840 cc.) of thick pus	Yes	Uneventful recovery; 2 yr. follow-up; roentgenogram normal
39	2 yr. M	Sudden onset of pain in left side of chest, followed by pneumonia and chronic empyema—Staph. albus	Homogeneous density with small rarefied areas	Empyema located between dome of diaphragm and under surface of left lower lobe; contained pus and necrotic material	Yes	Moderately stormy postoperative course; 2 yr. follow-up; child well
40	6 yr. M	Measles complicated by pneumonia and empyema; drainage followed by fever for 7 mo.	Encapsulated pleural effusion	After 5th day of admission, empyema drained; after 50 days second operation: small pulmonary abscess found and unroofed	Yes	Rapid cure following second operation; 3 yr. follow-up; child well

eases influenced slightly, if at all, by drug therapy. Evidence points to penicillin as a drug which at times exerts a specific effect on the disease. The etiologic importance of a particular staphylococcus in pneumonias of early infancy and the likelihood that any pneumonic lesion in a young infant is of staphylococcic origin are emphasized. The clinical manifestations are stressed, so that the diagnosis can be suspected early in the disease, at which time penicillin therapy is most effective.

The surgical complications of staphylococcic pneumonia are described. Timely surgical intervention for pleural complications can be life saving, particularly in cases of rapid accumulation of pus, with or without the addition of air. Closed drainage is advocated for such cases and temporizing methods are deplored. Attempts at sterilization of the pleural infection by penicillin are not advocated, because only unsatisfactory results have been noted in limited personal experiences. If local administration of penicillin for empyema is to be employed, it should be reserved for patients who are not suffering from severe toxemia and/or the mechanical effects of mediastinal displacement. Staphylococcic pulmonary abscess, to be anticipated rarely in the era of penicillin, is amenable to cure by correctly planned surgical drainage through viscero-parietal pleural adhesions.

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Case Reports

LIPID ANALYSIS IN A CASE OF NIEMANN-PICK DISEASE

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NIEMANN-PICK disease is a congenital lipid dyscrasia, frequently familial, in which certain phosphatides because of defective metabolisms tend to accumulate within the body. The excess phosphatide is phagocytosed by cells of the reticuloendothelial system, and these cells become amassed in various organs, mainly spleen, liver and lymph nodes. This condition, known by the names of the first contributors,[1] resembles Gaucher's disease, from which it is differentiated by the earlier age incidence, mortality occurring before the end of the second year, racial proclivities and the type of stored lipid. A definite differential diagnosis depends on the identification of the abnormally occurring lipids. Chemical analysis of the phospholipids in the liver and spleen of a patient dying of Niemann-Pick disease is reported in this paper.

Recent reviews by Baumann, Klenk and Scheidegger,[2] Atkinson[3] and Canmann adequately cover the clinical bibliography which is not repeated here. A total of 60 published cases of Niemann-Pick disease were listed by Canmann[4] in 1944. These studies contain clinical and histologic descriptions of the condition, but the organs of only 23 of the patients were subjected to even a partial lipid analysis. Chemical analyses were complete in only 9 of these 23 cases, of which 4 were reported by Klenk.[5]

Prior to the recognition by Pick in 1922[1b] of this disease as a clinical entity distinct from Gaucher's disease, Wahl and Richardson[6] had compared the lipid content of a normal liver and spleen with that of the same organs from a patient

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1. (*a*) Niemann, A.: Ein unbekanntes Krankheitsbild, Jahrb. f. Kinderh. **79**: 1-10, 1914. (*b*) Pick, L., cited by Siegmund.[7]

2. Baumann, T.; Klenk, E., and Scheidegger, S.: Die Niemann-Picksche Krankheit: Eine klinische, chemische und histopathologische Studie, Ergebn. d. allg. Path. u. path. Anat. **30**:183-323, 1936.

3. Atkinson, F. R. B.: Niemann-Pick's Disease, Brit. J. Child. Dis. **34**:245-272 (Oct.-Dec.) 1937.

4. Canmann, M. F.: Niemann-Pick Disease, J. Pediat. **24**:335-347 (March) 1944.

5. (*a*) Klenk, E.: Ueber die Natur der Phosphatide der Milz bei der Niemann-Pickschen Krankheit, Ztschr. f. physiol. Chem. **229**:151-156, 1934; (*b*) Ueber die Natur der Phosphatide und anderer Lipoide des Gehirns und der Leber bei der Niemann-Pickschen Krankheit, ibid. **235**:24-36, 1935; (*c*) Beiträge zur Chemie der Lipoidosen: Niemann-Picksche Krankheit und amaurotische Idiotie, ibid. **262**:128-143, 1939.

6. Wahl, H. R., and Richardson, M. L.: A Study of the Lipin Content of a Case of Gaucher's Disease in an Infant, Arch. Int. Med. **17**:238-259 (Feb.) 1916.

dying with a malady which they designated as Gaucher's. Although their methods and terminology differed from those used today, their results showed a definite increase of total lipids in the affected organs, especially in the fractions termed by them "lecithin" and "cholesterol and phosphatid." Siegmund,[7] in 1921, obtained analogous results with different methods of extraction methods. In view of the chemical results obtained, many later workers[8] have suggested that these investigators were actually dealing with Niemann-Pick disease.

Bloom and Kern[8b] reported that the amount of lipids obtained by ether and alcohol extraction of dried spleen from a patient with Niemann-Pick disease was greater than that of a dried normal spleen. Brahn and Pick,[9] Corcan, Oberling and Dienst,[10] Kramer[11] and Dienst[12] recorded similar observations. MacFate[13] autoclaved ground "Niemann-Pick" spleen with 2 per cent hydrochloric acid for two hours and then, by subsequent extraction with petroleum ether, obtained lipid values comparable to those of previous workers.

Epstein and Lorenz[14] first mentioned the occurrence of increased amounts of phosphatide other than lecithin in the "Niemann-Pick" spleen. These same authors,[15] using ether and alcohol successively as solvents on wet tissue, obtained similarly high lipid concentrations from "Niemann-Pick" brain, liver and spleen. The amount of the fraction which they termed "lecithin," calculated from the phosphorus content of this extract, would actually be that for both glycerophosphatides, because the ether fraction would contain lecithin, cephalin and any other phosphorus-containing compounds extractable from wet tissue by ether.

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7. Siegmund, H.: Lipoidzellenhyperplasie der Milz und Splenomegalie Gaucher, Verhandl. d. deutsch. path. Gesellsch. **18**:59-62, 1921.

8. (*a*) Pick, L.: Der Morbus Gaucher und die ihm ähnlichen Erkrankungen, Ergebn. d. inn. Med. u. Kinderh. **29**:519-627, 1926; cited by Holt, L. E., and Howland, J.: Holt's Diseases of Infancy and Childhood, ed. 11, revised by L. E. Holt Jr. and R. McIntosh, New York, D. Appleton-Century Company, Inc., 1940, p. 1354. (*b*) Bloom, W., and Kern, R.: Spleens from Gaucher's Disease and Lipoid Histiocytosis: The Chemical Analysis, Arch. Int Med. **39**:456-461 (March) 1927.

9. Brahn, B., and Pick, L.: Zur chemischen Organanalyse bei der Lipoidzelligen spleno-hepato-megalie Typus Niemann-Pick, Klin. Wchnschr. **6**: 2367-2369 (Dec.) 1927.

10. Corcan, P.; Oberling, C., and Dienst, G.: La maladie de Niemann-Pick, Rev. franç. de pédiat. **3**:789-829 (Dec.) 1927.

11. Kramer, B.: Lipoid-Cell Splenohepatomegaly, Niemann-Pick Type: A Clinical Analysis of Nine Cases with a Report of One Additional Case, M. Clin. North America **11**:905-918 (Jan.) 1928.

12. Dienst, G.: Ueber einen Fall von lipoidzelliger Splenohepatomegalie, Jahrb. f. Kinderh. **123**:181-199 (March) 1929.

13. MacFate, R. P.: A Chemical Analysis of Liver and Spleen from a Case of Lipoid-Histiocytosis, Arch. Path. **6**:1054-1057 (Dec.) 1928.

14. Epstein, E., and Lorenz, K.: Die Phosphatidzellverfettung der Milz bei Niemann-Pickscher Krankheit verglichen mit der Lipoidchemie des Morbus Gaucher und der Schüller-Christianschen Krankheit, Ztschr. f. physiol. Chem. **192**:145-170, 1930.

15. Epstein, E., and Lorenz, K.: Die Phosphatidzellverfettung in Gehirn, Leber und Milz bei Niemann-Pickscher Krankheit, Ztschr. f. physiol. Chem. **211**: 217-230, 1932.

It has been generally accepted,[16] as originally stated by Le Breton,[17] that phospholipid values calculated from ether-soluble phosphorus give figures which are too high. Determinations of the nondialyzable phosphorus content of the alcohol fractions indicated the presence of additional phosphatide. The authors concluded that there was an increase of ether-soluble lecithin, as well as ether-insoluble but alcohol-soluble phosphatides, in these organs.

Sobotka and his co-workers[18] used successively acetone, ether and alcohol in extracting the livers and spleens from 3 patients dying of Niemann-Pick disease, but although they analyzed the various fractions for cholesterol, nitrogen and phosphorus, no attempt was made to isolate each fraction. Espinos, Uribes and Vilaplana[19] and Canmann[4] reported lipid analyses performed by other investigators on organs from their patients. They gave no details of the chemical methods used.

A considerable advance in chemical characterization of the lipids of "Niemann-Pick" organs came with the identification of the alcohol-soluble phosphatide as sphingomyelin by Klenk[5] in reports appearing in 1934, 1935 and 1939. Klenk's initial extraction was made with acetone, followed by ether and then subsequently by a 3 to 1 mixture of methyl alcohol and chloroform. The glycerophosphatides, separated from the acetone and ether fractions by the calcium chloride method of Bloor and Snider,[20] were hydrolyzed, and the fatty acids from each fraction were isolated. The crude sphingomyelin was purified and its structure proved by hydrolysis with subsequent isolation and identification of the sphingosine and the component fatty acids. Tropp and Eckardt[21] and Chargaff,[22] employing the methods of Klenk,[5] and Teunissen[23] and Guccione,[24] using those of Epstein and Lorenz,[25] substantiated Klenk's observations.

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16. Bloor, W. R.: Biochemistry of the Fatty Acids, New York, Reinhold Publishing Corporation, 1943, p. 47.

17. Le Breton, E.: Sur la présence et le dosage dans le phosphore lipoïdique total éthérosoluble de composés phosphorés autres que les phosphatides, Bull. Soc. chim. biol. **3**: 539-546 (Nov.) 1921.

18. Sobotka, H.; Epstein, E., and Lichtenstein, L.: Die Lipoidverteilung bei der Niemann-Pickschen Krankheit, Klin. Wchnschr. **11**:1028-1031 (June) 1932; The Distribution of Lipoid in a Case of Niemann-Pick Disease Associated with Amaurotic Family Idiocy, Arch. Path. **10**:675-686 (Nov.) 1930. Sobotka, H.; Glick, D.; Reiner, M., and Tuchman, L.: The Lipoids of the Spleen and Liver in Various Types of Lipoidosis, Biochem. J. **27**:2031-2034, 1933.

19. Espinos, D.; Uribes, M., and Vilaplana, E.: Contribución al estudio de las histiocitomatosis por impregnación lipoidica (tipo Niemann-Pick), An. de med. int. **5**:307-351 (April) 1936.

20. Bloor, W. R., and Snider, R. H.: The Neutral Fats of Beef Liver and Other Tissues, J. Biol Chem. **87**:399-413 (June) 1930.

21. Tropp, C., and Eckardt, B.: Spingomyelin bei Niemann-Pickscher Krankheit, Ztschr. f. physiol. Chem. **243**:38-42, 1936.

22. Chargaff, E.: Study of the Spleen in a Case of Niemann-Pick Disease, J. Biol. Chem. **130**:503-511 (Oct.) 1939.

23. Teunissen, P. H.: Beitrag zur Kenntnis der Chemie der Lipoidosis phosphatidica, Ztschr. f. physiol. Chem. **248**:142-150, 1937.

24. Guccione, F.: Su di una particolare forma di spleno-epatomegalia tipo Niemann-Pick, Pediatria **44**:757-790 (Sept.) 1936.

25. Epstein and Lorenz.[14] Epstein and Lorenz. [15]

In summary, to date the abnormally occurring lipids in organs of patients dying with Niemann-Pick disease have been shown to consist of two phosphatide fractions, the glycerophosphatides and sphingomyelin. The sphingomyelin has been isolated in a pure form and its constituents identified. The two glycerophosphatides, lecithin and cephalin, have not been isolated separately.

REPORT OF A CASE

Clinical History.—The patient, J. A. B., a white boy 9 months of age, was admitted to the Children's Hospital of Pittsburgh on May 8, 1944, on the service of Dr. J. L. Foster. This child had had metabolic disturbances with distention of the abdomen and vomiting since birth. On admission he weighed 15 pounds (6,803 Gm.) and showed maldevelopment and inability to sit up and hold up his head. The muscular development of the extremities was poor. The eyes showed no abnormality except nystagmus. There were no palpable lymph nodes. On palpation and auscultation the lungs and the heart appeared normal. The musculature of the distended abdomen was so tense that the liver and spleen could not be felt. The laboratory tests revealed nothing remarkable except for a low blood calcium. Monocytes with phagocytosed lipid were not found in blood smears.

Bronchitis developed after two days' stay in the hospital, at which time the liver could be palpated 4 cm. below the costal margin. The tip of the spleen could be felt. Later gastroenteritis developed which was improved by sulfathiazole in a dosage of 323 grains (21 Gm.). A transfusion of 100 cc. of whole blood and a second one of 80 cc. of plasma were given. The patient's temperature throughout his stay in the hospital ranged between normal and 106 F.

The child was discharged from the hospital June 19 and died at home on June 25.

It was through the agency of Dr. J. L. Foster that we were given the opportunity of performing a necropsy.

A letter to Dr. J. L. Foster from Dr. L. Homer Smith of Portland, Ore., on June 17, 1944, gave the gross anatomic findings on a 19 month old sibling who had died in the Doernbecker Hospital of that city in September 1940 with a diagnosis of lipid storage disease, probably Niemann-Pick.

Report of Necropsy.—Permisson was granted only for an abdominal examination. The outstanding findings were marked enlargement of spleen, liver and peritoneal lymph nodes. The liver weighed 965 Gm. and extended 8 cm. below the costal margin. This organ had a pale yellowish color. The cut surface was pale and bloodless but did not appear greasy. The spleen, weighing 240 Gm., was surrounded by a taut, smooth capsule and was of a pale ivory color with a faint red mottling. The cut surface was similarly mottled. A small accessory spleen, 1 cm. in diameter, had the same appearance as the main organ. The mesenteric nodes were increased in size, the largest measuring 15 by 10 by 6 mm. On section, the cut surface appeared waxy. A smear from the pale yellowish bone marrow of rib showed great numbers of monocytes filled with a pale substance which failed to stain directly with sudan IV. Through a short incision in the diaphragm, a small section of the lung was removed.

Microscopically, spleen, liver and lymph nodes showed massive infiltration throughout with large mononuclear cells distended with a colorless substance which did not stain with the ordinary fat stains. The alveoli and the alveolar walls of the lungs and the bone marrow contained many similar cells.

The age of the patient, together with the history and anatomic observations, warranted a diagnosis of lipid histocytosis of the Niemann-Pick type. This was confirmed by chemical analysis.

CHEMICAL METHODS

The water content of fresh tissue of the spleen and the liver was determined on a small portion removed from each organ. The tissue of the liver used for analysis weighed 200 Gm., and of the spleen 175 Gm. Both of these portions of the organs were immediately placed in acetone. The tissues were minced in a Waring blender with acetone, and the ground tissue was then placed in paper thimbles and extracted in a Soxhlet apparatus successively, three times with acetone (A 1), twice with ether (E 1) and twice with an equal mixture of methyl alcohol and chloroform (M-C 1). Similar extracts (of A 1, E 1 and M-C 1) were pooled for further analyses. The tissue residue was dried and weighed.

The three residues obtained from the extracts (A 1, E 1 and M-C 1) of each organ by vacuum distillation were extracted three times with cold ether (E 2) and then with the mixture of methyl alcohol and chloroform (M-C 2). Both of these extracts (E 2 and M-C 2) were dried and weighed.

The cold ether extract (E 2) contained mainly lecithin, cephalin, neutral fats, cholesterol and cholesterol esters. The two lipids, lecithin and cephalin, were separated by the Bloor[26] method, and were purified according to the procedures of Levene and Rolf.[27] The neutral fat, cholesterol and cholesterol esters from this fraction (E 2) were combined, dried and weighed.

The dried methyl alcohol-chloroform (M-C 2) extract, termed "crude sphingomyelin," contained sphingomyelin and cerebrosides. The sphingomyelin was purified by the method of Levene.[28] Attempts were made to recover the cerebroside from the extract (M-C 2), but such small amounts were obtained that it was not possible to perform a chemical analysis. The purified lecithin, cephalin and sphingomyelin fractions from both the liver and spleen were analyzed for nitrogen by the Pregl micro-Kjeldahl procedure,[29] with certain modification,[30]

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26. Bloor,[20] pp. 42 and 44.

27. Levene, P. A., and Rolf, I. P.: The Preparation and Purification of Lecithin, J. Biol. Chem. **72**:587-590 (April) 1927; Note on the Preparation of Cephalin, ibid. **74**:713-714 (Sept.) 1927.

28. Levene, P. A.: On Sphingomyelin, J. Biol. Chem. **18**:453-462, 1914.

29. Pregl, F.: Quantitative Organic Microanalysis, translated by E. B. Daw, Philadelphia, P. Blakiston's Sons & Company, Inc., 1937, p. 86.

30. An all glass modification was patterned after the apparatus described by W. F. Goebel (in Peters, J. P., and Van Slyke, D. D.: Quantitative Clinical Chemistry, Baltimore, Williams & Wilkins Company, 1932, vol. 2, pp. 530-532). The digestion mixture used was that described in the Arnold-Gunning method (Peters and Van Slyke, p. 527) plus selenious acid. The ammonia was distilled into boric acid containing a double indicator (Sobel, A. E.; Yuska, H., and Cohen, J.: A Convenient Method of Determining Small Amounts of Ammonia and Other Bases by the Use of Boric Acid, J. Biol. Chem. **118**:443-446 [April] 1937) and was titrated with seventieth-normal acid (Peters and Van Slyke, p. 530) and for phosphorus by the Kuttner and Lichtenstein method (Kuttner, T., and Lichtenstein, L.: Micro Colorimetric Studies: III. Estimation of Organically Bound Phosphorus; a System of Analysis of Phosphorus Compounds in Blood, J. Biol. Chem. **95**:661-670 [March] 1932.).

31. This footnote has been deleted.

RESULTS

The water content of the tissues was determined in order to make comparisons on the basis of dry weight. The liver contained 70.34 per cent and the spleen 70.77 per cent water.

The lipid constituents extracted from these organs were lecithin, cephalin, neutral fats, cholesterol, cholesterol esters, sphingomyelin and cerebrosides. After completion of the extraction procedure, the liver residue weighed 25.6 Gm. and

TABLE 1.—*Lipid Fractions Isolated (Amount Expressed in Grams)*

	Liver		Spleen	
	Crude Fractions	Purified Fractions	Crude Fractions	Purified Fractions
Lecithin	7.8	0.7	5.1	*
Cephalin	2.5	0.5	1.8	0.6
Sphingomyelin	16.8	9.1	16.9	7.6

* A portion of the purified lecithin fraction isolated from the spleen was accidentally lost, although enough remained for determinations of nitrogen and phosphorus.

the spleen residue weighed 21.3 Gm. The combined neutral fat and cholesterol fractions of the liver and the spleen weighed 10.5 Gm. As previously mentioned, the crude cerebroside fraction isolated was too small for purification or chemical analysis.

The amounts of lecithin, cephalin and sphingomyelin obtained are shown in table 1.

TABLE 2.—*Comparison of Results of Our Lipid Analyses with Those Reported by Other Investigators (Expressed as Percentage of Dry Weight)*

	Liver Lipid Fractions			Spleen Lipid Fractions		
	Normal Tissue *	Maximal and Minimal Values Recorded by Other Workers †	Values Obtained in Our Case, (J. A. B.)	Normal Tissue *	Maximal and Minimal Values Recorded by Other Workers ‡	Values Obtained in Our Case, (J. A. B.)
Lecithin	4.81	.....	13.0	3.54	.....	9.7
Cephalin	4.62	.....	4.1	4.16	.....	3.4
Combined glycerophosphatides	9.43	5.98 - 19.67	17.1	7.70	4.06 - 13.17	13.1
Crude sphingomyelin	0.38	13.68 - 33.8	28.0	0.86	9.33 - 34.2	32.1
Purified sphingomyelin §	....	10.5 - 23.1	15.1	....	2.6 - 22.8	14.4

* These figures were reported by Thannhauser and his co-workers.[32]

† Figures from reports of Klenk,[5bc] Epstein and Lorenz,[15] Tropp and Eckardt [21] and Teunissen.[23]

‡ Figures from reports of Klenk,[5ac] Epstein and Lorenz,[14] Tropp and Eckardt,[21] Gucclone,[24] Teunissen [23] and Chargaff.[22]

§ Maximal and minimal figures recorded for liver quoted from Klenk,[5bc] Tropp and Eckardt [21]; for spleen quoted from Klenk,[5ac] and Chargaff.[22]

A comparison of our results with those for normal liver and spleen [32] and with those reported by other investigators for "Niemann-Pick" organs is shown in table 2. The striking feature shown in these two tables is the large amount

32. Thannhauser, S. J.; Benotti, J.; Walcott, A., and Reinstein, H.: Studies on Animal Lipids: The Lecithin, Cephalin and Sphingomyelin Content of Normal Human Organs, J. Biol. Chem. **129**:717-719 (Aug.) 1939.

of lecithin and sphingomyelin in the "Niemann-Pick" tissues, especially when compared with the values of these fats for normal liver and spleen as reported by Thannhauser and his co-workers.[32]

The nitrogen and phosphorus content of the purified fractions and the calculated nitrogen: phosphorus ratios are shown in table 3.

TABLE 3.—*Results of Chemical Determinations on Lipid Fractions*

	Nitrogen, Percentage of Dry Weight	Phosphorus, Percentage of Dry Weight	Nitrogen-Phosphorus Ratios
Liver fractions			
Lecithin	1.54	3.41	1:0.99
Cephalin	1.63	3.51	1:0.96
Sphingomyelin	3.57	3.85	2.1:1
Spleen fractions			
Lecithin	1.53	3.12	1:0.92
Cephalin	1.73	3.99	1:1.04
Sphingomyelin	3.61	3.83	2.1:1

The ratios closely approximate the theoretic values of 1:1 for lecithin and cephalin and 1:2 for sphingomyelin.

COMMENT

In agreement with other workers we have found increased amounts of glycerophosphatides and sphingomyelin in the liver and spleen of a patient dying with Niemann-Pick disease. However, according to our analysis the increase in the glycerophosphatides is due almost entirely to the excess of the lecithin portion, as cephalin occurs within normal limits. This finding is contrary to the report of Chargaff [22] who, on the basis of amino nitrogen determinations on the glycerophosphatide fraction, calculated that cephalin constituted 82 per cent of the fraction. To the best of our knowledge, our separate isolation of the two glycerophosphatides, lecithin and cephalin, is the first to be reported in a case of Niemann-Pick disease.

If the methods used by us to separate the three phosphatides are adequate, the abnormal metabolism in Niemann-Pick disease concerns mainly sphingomyelin and lecithin, and especially the sphingomyelin. The cephalin apparently is not involved in the disturbed metabolism. The presence of choline and phosphoric acid in both lecithin and sphingomyelin suggests that the defective lipid metabolism in this disease may be concerned primarily with the choline-phosphoric acid portion of these two phosphatides.

A persistent disturbance of lipid equilibrium in the organism leads to a storage of any excess unmetabolized lipid in the reticuloendothelial system. The experimental reproduction of deposition in the tissue of monocytic cells loaded with phagocytosed lipids as occurs in Niemann-Pick disease was obtained in dogs by Beumer and Gruber [33] and in rabbits by Ferraro and Jervis,[34] following intra-

33. Beumer, H., and Gruber, B.: Versuche zur experimentellen Erzeugung der Niemann-Pickschen Krankheit, Jahrb. f. Kinderh. **146**:125-130 (Feb.) 1936.

34. Ferraro, A., and Jervis, G. A.: Studies in Experimental Lipoidoses: I. Phosphatides, Arch. Path. **30**:731-744 (Sept.) 1940.

venous injections of sphingomyelin. Tompkins,[35] after intravenous injections of lecithin in rabbits, obtained a similar but modified picture. As already discussed by Ferraro and Jervis,[34] the histologic picture explains the method for disposal of the excess phosphatide by the body but does not explain the activating cause of the disturbance.

CONCLUSION

The amounts of total glycerophosphatides and sphingomyelin, found by chemical analyses of liver and spleen from a child dying of Niemann-Pick disease, were comparable to those previously reported. The lecithin and sphingomyelin were abnormally high and the cephalin was normal in amount.

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35. Tompkins, E. H.: Effects of Repeated Intravenous Injections of Lecithin in Rabbits, Arch. Path. **35**:695-712 (May) 1943.

APHASIA AFTER MENINGITIS

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APHASIA is a relatively rare condition. As a rule it develops in persons beyond middle age, as a result of hemorrhages, tumors or other conditions in the brain. Aphasia in children is rare; therefore, 1 unusual case is here recorded.

C. A. P., a 12 year old white girl, was admitted to the Columbia hospital after having been sick for only two or three days. Her complaints were general malaise, headaches and fever; previous to this illness she had always been in good health. At admission her temperature was 102 F. The spinal fluid had a cloudy appearance and a cell count of 100. It contained globulin, but not sugar, and there were meningococci present. The blood contained 75 Gm. of hemoglobin per hundred cubic centimeters and 20,000 white blood cells, with 90 per cent neutrophilic polymorphonuclear cells and 10 per cent lymphocytes. The sedimentation rate was 20 mm. after thirty minutes and 45 mm. after one hour. She received 15,000 units of penicillin every three hours, a total of 500,000 units. On the second day after her admission her temperature in the morning was 103 F., and on the fourth day it was normal. Her general condition improved and the stiffness of the neck disappeared rapidly. On the third and fourth days the pediatrician noticed that the patient was unable to hear. Therefore consultation of an otologist was ordered.

The examination of eyes, ears, nose and throat at this time revealed no abnormality with the exception of a slight hyperemia of the left ear drum. The upper posterior quadrant of the drum had a number of blood vessels radiating toward the center. Since the patient was in the isolation ward it was impossible to perform a hearing test. She was unable to hear any sound at all, not even loud clapping of the hands close to either ear or the whistle of a train which passed her window. At this time the tentative diagnosis of nerve deafness due to meningitis was made. On July 3, 1945, the seventeenth day after her admission to the hospital, an audiogram showed a complete loss of hearing in both ears with the exception of remnants of hearing at 256 double vibrations (fig. 1). She then received treatment with vitamins and was sent to her country home. On August 23 and later, on December 3, audiograms were taken which showed a return of her ability to hear with a pure tone audiometer, but a nerve type of deafness remained. At this time it was decided to try the use of a hearing aid, since the loss of perception permitted the assumption that such an aid would be of some benefit. However, the hearing aid did not enable the patient to understand a spoken word, although she said that she could hear the "noises" rather well at that time. Therefore the diagnosis had to be changed to one of sensory aphasia.

In this case of "word deafness" the patient is able to write and read and is also able to talk normally without making any mistakes at all. However, she cannot understand a spoken word, although she can hear well with the help of a hearing aid. This rare type of pure sensory aphasia in a right-handed person must be due to an involvement of the left subcortical region in the temporal lobe.[1]

1. (*a*) Bing, R.: Compendium of Regional Diagnosis in Lesions of the Brain and Spinal Cord, ed. 11, St. Louis, C. V. Mosby Company. (*b*) Spiegel, E. A., and Sommer, I.: Neurology of Eye, Ear, Nose and Throat, New York, Grune & Stratton, Inc., 1944, p. 573.

There are different centers in the brain for language (fig. 2), Broca's center for the expression of speech, Wernicke's center for the reception of speech, and one center for reception of writing and one for expression of writing.[1b] All these centers [1a] are of course connected with one another as well as with the auditory and optic nerve centers and with the higher psychic centers. A cortical lesion never produces pure aphasia because it interrupts some of the association fibers. A subcortical

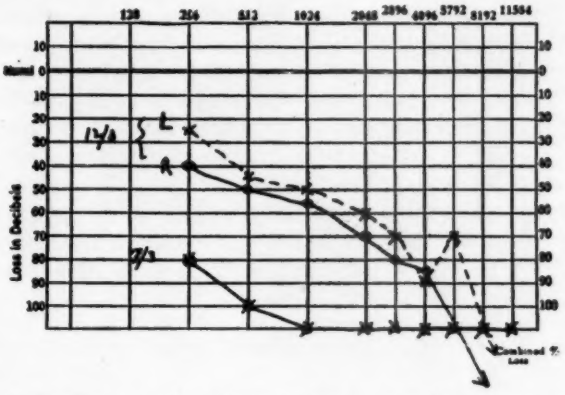

Fig. 1.—Audiogram showing complete loss of hearing except at 256 double vibrations on July 3, and some recovery of hearing on December 3.

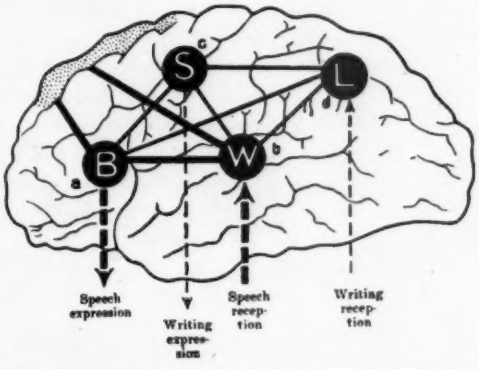

Fig. 2.—The cortical speech centers and their connections. Shaded area shows center for correlation of perception. *B*, Broca's center; *L*, center for reading; *W*, Wernicke's center; *S*, center for writing; *a*, inferior frontal gyrus; *b*, superior temporal gyrus; *c*, precentral gyrus; *d*, angular gyrus.

(Reproduced from Bing [1a] with permission of the publisher.)

lesion, on the other hand, which undermines but does not involve the cortex, causes pure aphasia. The lesions of the temporal lobe produce a pure sensory or "word deafness." In such a case paraphasia (the use of similar sounding but incorrect words) is absent because the fibers to the cortex are not interrupted. In cases in which Wernicke's center is involved, however, paraphasia is always present. This apparently explains the pathologic changes in this case.

In the literature no reference to a single case could be found. Taillens [2] reported aphasia in children resulting in one case from polioencephalitis, in another from acute encephalitis and in a third from pneumonia and subsequent streptococcic abscess. F. P. Weber [3] reported on a patient with conjectural word deafness. E. Fröschels [4] wrote an interesting report on aphasia in children and their treatment. A. Levinson [5] in his monograph about meningococcic meningitis did not mention aphasia as a complication of this disease. The fact that cases of such aphasia are not reported in the literature but complete deafness on the other hand is a widely known complication of meningitis is somewhat surprising. It must be considered that at least some of the patients with complete deafness due to involvement of the auditory nerve may really have had aphasia. Exact studies with a pure tone audiometer may have shown results similar to the results reported here.

SUMMARY

Sensory aphasia (pure word deafness) is reported as the sequel of a case of meningococcic meningitis. The question is raised whether the cases of complete deafness reported to result from this disease would be diagnosed as cases of aphasia if thorough audiometric studies were made.

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2. Taillens, J.: L'aphasie chez les enfants, Schweiz. med. Wchnschr. **67**:988 (Oct. 9) 1937.

3. Weber, F. P.: Congenital Deficiency of Conscious Auditory Perception of Words, Proc. Roy. Soc. Med. **26**:509 (March) 1933.

4. Fröschels, E.: Ueber Aphasien im Kindesalter und über die logopädische Therapie von Aphasien, Med. Klin. **24**:446 (March 23) 1928.

5. Levinson, A., in Brennemann, J.: Practice of Pediatrics, Hagerstown, Md., W. F. Prior Company, Inc., vol. 4, chap. 8, p. 54.

CONGENITAL HEMOLYTIC ANEMIA—A CASE REQUIRING EARLY SPLENECTOMY

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RECENT reviews of congenital hemolytic anemia in childhood have been published by Abt, Debré, Diamond and others,[1] all of whom emphasize the mild and atypical manifestations in early infancy.

This disease has been recognized by the third day of life (Hawksley[2]), the diagnosis having been made on the basis of family history, increased fragility of the red blood cells and microcytosis. However, jaundice and splenomegaly did not appear until the infant was over a month of age.

The following report of a case is presented because of the early age at which the classical evidence of congenital hemolytic anemia appeared, necessitating the patient's admission to the hospital at the age of 17 days, followed by splenectomy at 10 weeks.

REPORT OF A CASE

History.—L. P., a 17 day old white boy, was admitted to Duke Hospital Sept. 6, 1945, because of jaundice of two days' duration. He was an only child, and there was no family history of blood dyscrasia or jaundice. However, during pregnancy the mother had received iron for a mild anemia. The infant was full term, delivery was normal, and the birth weight was 2,955 Gm. The mother thought that he was "dark complexioned" at birth, though he soon became pale. He had a mild bout of diarrhea while in the hospital, but after this he did well until two days before admission to Duke Hospital, when he became icteric and vomited several times.

Physical Examination.—The child's temperature was 36.6 C. (97.9 F.) and his weight was 3,250 Gm. He was active and had a strong cry. His skin and scleras were pale yellow. The sutures and fontanelles were normal for his age. The upper respiratory tract was not remarkable. The lymph nodes were not enlarged. The heart did not seem large on percussion, and the rhythm was

From the Department of Pediatrics, Duke University School of Medicine and Duke Hospital, Durham, N. C.

1. Abt, A. F.: Hemolytic Disease in Infants, Am. J. Dis. Child. **60**:812 (Oct.) 1940. Debré, R.; Lamy, M.; See, G., and Schrameck, G.: Congenital and Familial Hemolytic Disease in Children, Am. J. Dis. Child. **56**:1189 (Dec.) 1938. Diamond, L. K.: Congenital Hemolytic Anemia in Infancy and Childhood, M. Clin. North America **21**:401 (March) 1937. Parsons, L. G.: The Hemolytic Anemias in Childhood, Lancet **2**:1395 (Dec. 17) 1938. Schiff, E.: Congenital Haemolytic Anaemia with Normal Fragility of the Red Blood Cells, Arch. Dis. Childhood **13**:264 (Sept.) 1938. David, J. K., Jr., and Minot, A. S.: Hemolytic Anemia in Infancy: Report of a Case with Determination of Hemolytic Activity of Serum, Am. J. Dis. Child. **68**:327 (Nov.) 1944.

2. Hawksley, J. C.: Acholuric Family Jaundice in an Infant, Proc. Roy. Soc. Med. **27**:942 (Feb.) 1934.

normal, but there was a rough, though soft, systolic murmur at the apex. The lungs were clear. The edge of the liver was felt, smooth and firm, about 2 cm. below the costal margin. The spleen, also smooth and firm, was palpated about 5 cm. below the costal margin. The genitalia, extremities and reflexes were normal.

Laboratory Data.—The hemoglobin was 5.4 Gm. per hundred cubic centimeters, there were 1,920,000 red blood cells, and the hematocrit reading was 12.5. The mean cell volume was 78 cubic microns. There were 20,350 white blood cells, with 26 per cent segmented polymorphonuclear cells, 2 per cent stab polymorphonuclear cells, 6 per cent eosinophils, 2 per cent myelocytes, 41 per cent small lymphocytes, 2 per cent large lymphocytes and 12 per cent monocytes. In a test of fragility of red blood cells hemolysis began in a 0.48 per cent solution of sodium chloride (as compared with a 0.38 per cent solution for an 11 day old control) and was complete in a 0.34 per cent solution (as compared with a 0.32 per cent solution for the control). Blood smears showed pronounced anisocytosis and poikilocytosis with a few macrocytes and many microcytes. Many of the small cells were spherical, and 60 per cent of the red blood cells were reticulocytes. There were 8 normoblasts and 28 erythroblasts per hundred white blood cells. The platelets appeared diminished. The blood was Landsteiner type A, Rh positive. The blood Kahn, Kline and Mazzini reactions were negative. The serum van den Bergh reaction was indirect, with the bilirubin elevated to 9.39 mg. per hundred cubic centimeters. The urine was normal and showed no bilirubin.

Course.—The child was given repeated blood transfusions until his hemoglobin reached 11.8 Gm., and was then discharged. The microscopic blood picture was unchanged.

Examination of the Family.—The mother was found to have a palpable spleen, and blood studies on her revealed 10.2 Gm. hemoglobin per hundred cubic centimeters, 3,500,000 red blood cells and a mean cell volume of 79 cubic microns. The fragility of the mother's red blood cells was tested. Hemolysis began in a 0.52 per cent solution of sodium chloride (as compared with a 0.42 per cent solution for a control) and was complete in a 0.40 per cent solution (as compared with a 0.32 per cent solution for the control). The mother's red blood cells varied more than normally in size and shape, and many were spherical. Two serum van den Bergh reactions were indirect. The bilirubin levels were 1.7 and 2.35 mg. per hundred cubic centimeters. Her blood was Landsteiner type O, Rh positive.

The maternal grandfather's spleen was not palpable, and he had no anemia or abnormally shaped red blood cells. However, his fragility test gave these results: Hemolysis began in a 0.56 per cent solution of sodium chloride (as compared with a 0.46 per cent solution for a control) and was complete in a 0.30 per cent solution (as compared with a 0.32 per cent solution for the control).

The maternal grandmother's spleen could not be felt and her blood was normal. The paternal family could not be examined.

Second Admission.—On October 29, at the age of 9 weeks, the infant was readmitted because of increasing pallor. His weight was now 4,680 Gm. No jaundice had been noted since the last admission, but examination showed the patient to be rather pale. The relative size of the spleen had not changed, but the liver was no longer palpable. The cardiac murmur had disappeared, and the heart was of normal size.

Laboratory Data.—The hemoglobin was 7.4 Gm. per hundred cubic centimeters, there were 2,900,000 red blood cells, and the hematocrit reading was 17. The mean cell volume was 65 cubic microns. There were 24,000 white blood

cells. The results of the fragility test were as follows: Hemolysis began in a 0.52 per cent solution of sodium chloride (as compared with a 0.42 per cent solution for a control) and was complete in a 0.42 per cent solution (as compared with a 0.34 per cent solution for the control). The blood smear again showed many spherocytes, and there were 20 nucleated red blood cells per hundred white blood cells.

Course.—Following several blood transfusions, a splenectomy was done. Convalescence was uneventful, and the infant was discharged two weeks after operation, with 11.5 Gm. of hemoglobin per hundred cubic centimeters. The spleen weighed 40 Gm., and microscopic sections through it revealed only an increase of iron pigment and fibrosis in the sinusoidal tissues.

Follow-up.—When seen again, on Jan. 22, 1946, the patient appeared robust and was developing normally. Blood studies revealed 11.8 Gm. of hemoglobin per hundred cubic centimeters, 4,100,000 red blood cells and a hematocrit reading of 32.7. The mean cell volume was 79 cubic microns. There were 10,500 white blood cells. Results of a fragility test were as follows: Hemolysis began in a 0.68 per cent solution of sodium chloride (as compared with a 0.46 per cent solution for a control) and was complete in a 0.32 per cent solution (as compared with a 0.32 per cent solution for the control). The red blood cells still showed anisocytosis and poikilocytosis, with numerous spherocytes. However, only 2 per cent were now reticulocytes.

SUMMARY

A report on a 17 day old infant with congenital hemolytic anemia in a crisis is presented. Anemia, jaundice and splenomegaly were present, and studies of the red blood cells showed many microcytes and spherocytes with a pronounced increase in fragility to hypotonic solution of sodium chloride. Investigation uncovered a mild, asymptomatic form of the disease in the mother and increased fragility of the maternal grandfather's red cells. The child's hemoglobin fell so rapidly after transfusion that splenectomy was thought to be indicated. This was done when he was 2½ months old, and at 5 months of age the infant is clinically well, though the abnormalities in his red blood cells have persisted.

Dr. Angus McBryde and Dr. Jay M. Arena gave valuable criticism during the course of these studies.

Progress in Pediatrics

AURICULAR FLUTTER WITH BLOCK IN CHILDREN

B. HOYER, M.D., and R. A. LYON, M.D., CINCINNATI

AURICULAR flutter with associated auriculoventricular block is one of the less common forms of paroxysmal tachycardia. In the medical literature of the past thirty years, only 10 reports of this condition in infants and children could be found. In the patient whom we observed the arrhythmia apparently developed shortly after birth, and he recovered spontaneously when he reached the age of 4 months. During this period only mild symptoms of circulatory failure were noted, and except for a slight trauma of the neck at birth no abnormality to explain the development of the condition could be detected. The course of the illness in this patient is described in detail, and the salient features of the disease in the patients previously reported on are discussed briefly.

REPORT OF A CASE

The patient was a white boy born March 8, 1945. The mother had had severe arthritis three years before this, her second, pregnancy, but she had recovered completely and had no clinical evidence of cardiac disease. The father was living and well, and one other child, a girl 4½ years of age, had been entirely well since birth.

During pregnancy, the mother had had several attacks of sinusitis requiring surgical treatment and had suffered mildly from nausea and vomiting throughout the entire nine months.

The birth history was unusual. Rupture of the membranes was the first indication to the mother of the onset of labor. Within a short time she experienced one severe pain which lasted about twenty minutes, until she was put under ether anesthesia. Less than a half-hour later she was delivered with the aid of forceps, and some difficulty was encountered in the extraction of the infant's shoulders.

The patient's birth weight was 10 pounds and 10 ounces (4,820 Gm.). A collar of edema was noted about the neck on both sides and posteriorly but not over the anterior portion. There was no discoloration of the skin, and the obstetrician thought the condition was probably due to subcutaneous hemorrhage. This swelling gradually subsided during the next eight weeks. At birth, the infant breathed rapidly but was not cyanotic. During the first two weeks of life he occasionally gasped for breath, and these attacks of dyspnea would sometimes wake him from sleep. The symptoms recurred throughout his illness. He nursed

From the Children's Hospital Research Foundation and the Department of Pediatrics, University of Cincinnati.

well but for only a few minutes at a time, and he often vomited small portions of his feedings. He was fed frequently during the day. On the sixth day of life the infant's pulse rate was noted to be rapid, and at every examination during the next month the tachycardia was noted. Since the infant's symptoms were less noticeable and he was gaining weight, no special examinations were made at this time.

When he was 7 weeks of age, an electrocardiogram was made, and the nature of the tachycardia was discovered. The ventricular rate was 210 per minute; the auricular rate was 400, and between the QRS complexes the base line was in continuous motion with no isoelectric periods (fig. 1). A diagnosis of auricular flutter with a 2:1 block was made, and the infant was sent to the hospital for observation and treatment.

At the time of his admission to the hospital, on May 14, 1945, the infant, now approximately 2 months of age, appeared to be well. He weighed 13 pounds (5,897 Gm.) and nursed well; his color was normal and he played actively when

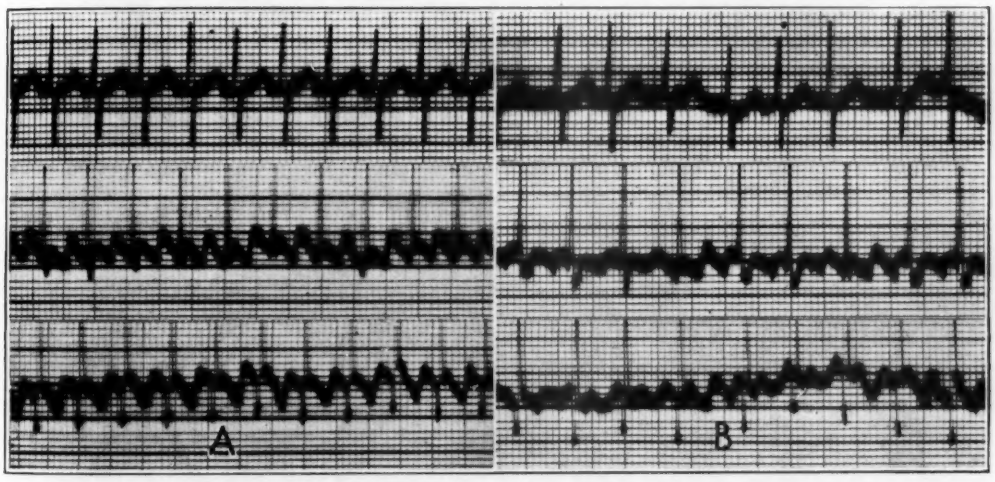

Fig. 1.—*A*, electrocardiogram taken April 28, 1945, age of patient 7 weeks, auricular rate 430, ventricular rate 220. *B*, electrocardiogram taken May 26, 1945, age of patient 2½ months, auricular rate 410, ventricular rate 190.

awake. The edema or induration about the neck had almost entirely subsided. The liver was not enlarged. The heart was normal except for the tachycardia, and there were no murmurs. Roentgenograms showed slight enlargement of the ventricular area and an increase of the width of the shadow at the base, but this was not considered incompatible with the normal cardiac configuration at this age (fig. 2). The cardiac rate varied from 150 to 200 per minute, and repeated electrocardiograms showed auricular flutter with a constantly maintained 2:1 block. The auricular rate varied from 410 to 430 and the ventricular rate from 190 to 220 per minute. Pressure on the eyeballs and over the carotid sinus areas produced no slowing of the cardiac rate; in fact, such procedures seemed to irritate the infant so that he cried and struggled and the cardiac rate increased.

Before the diagnosis had been made, neostigmine bromide had been given without effect. After the diagnosis was established, digifolin in doses of 0.5 cc.

of ampule solution was injected every six hours for four days. This drug seemed to produce some irregularity of cardiac action, consisting of periods of slower rate followed by rapid ones. No evidence of auricular fibrillation was detected clinically or in the electrocardiograms. Fear of producing a higher degree of auriculoventricular block led to discontinuance of the drug, and the patient was sent home for a period of time.

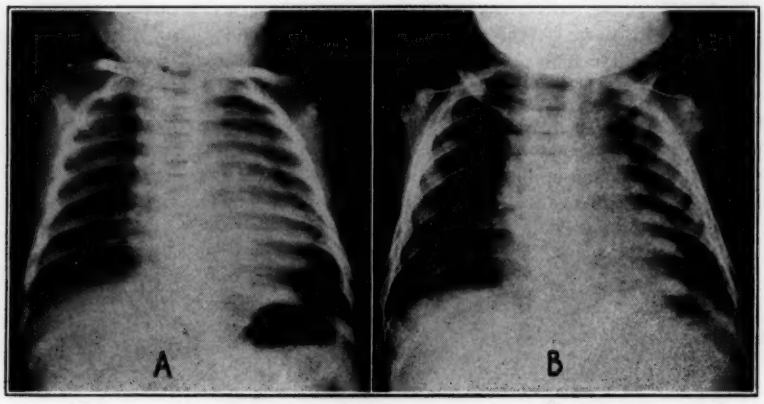

Fig. 2.—*A*, teleoroentgenogram taken May 26, 1945, age of patient 2½ months; *B*, teleoroentgenogram taken Aug. 15, 1945, age of patient 5 months.

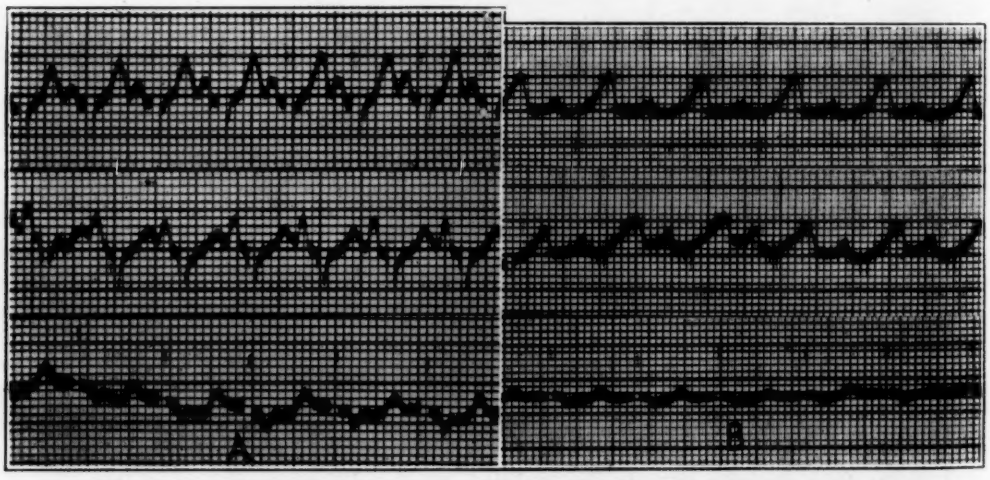

Fig. 3.—*A*, electrocardiogram taken July 3, 1945, age of patient 4 months, normal rhythm, cardiac rate 180; *B*, electrocardiogram taken Aug. 15, 1945, age of patient 5 months, normal rhythm, rate 130.

On July 2, 1945 when the patient was a little less than 4 months of age, he was readmitted to the hospital for another attempt to restore normal rhythm by the administration of a second course of digitalis. During the five week period at home the infant had gained only a few ounces of weight and had been in good health except for occasional gasping spells and slight vomiting. He sometimes

seemed pale and restless, but never was he cyanotic. The mother had noticed that a sudden change of the position of the patient such as quickly picking him up or putting him down seemed to make him pale and listless for a few minutes. The pulse rate had continued to be rapid, but on the night before admission to the hospital the mother observed that the rate was slower than it had ever been before. The next morning, the rate was found to be 130 beats per minute. An electrocardiogram was taken at once and on the following day, but on both occasions the infant cried, so that the recorded rate varied from 160 to 180. The auricular flutter had disappeared, however, leaving a normal sinus rhythm. The patient was discharged without any medication having been given (fig. 3).

Six weeks later (Aug. 15, 1945), at the age of 5 months, the patient returned for observation. He had been in good health and had gained weight slowly, and all abnormal symptoms had disappeared. The average pulse rate at home varied from 120 to 130. Electrocardiograms at this time showed a rate of 130, a normal rhythm and inversion of the T waves in lead III (fig. 3).

On Jan. 16, 1946, when the patient was 10 months of age, he was in good health, and the electrocardiogram was similar to that of Aug. 15, 1945.

COMMENT

The diagnosis of auricular flutter is difficult to make with certainty in children. The condition is closely related to paroxysmal auricular tachycardia in all of its manifestations. Diagnostic criteria of flutter [1] have included the rapid auricular rate, a tendency of the condition to recur in attacks with the same rapid rate, failure of the heart to resume a normal rhythm following vagal stimulation, frequent occurrence of auriculoventricular block and finally the appearance of the waves in the electrocardiogram. In the case of auricular flutter, there is a continuous up and down motion of the waves between the QRS complexes, with absence of any isoelectric periods. In the opinion of some authors [2] the diagnosis of auricular flutter must be based primarily on the last-mentioned finding, while others [3] have contended that various types of tachycardia in which both the P and T waves are present may present such a picture.

In view of the difficulties of diagnosis, some confusion exists in the literature with respect to the classification of these forms of tachycardia. In the cases of the 10 patients whose records we have selected to review,

1. (*a*) Lewis, T.: Lectures on the Heart, New York, Paul B. Hoeber, 1915, p. 116. (*b*) Shookhoff, C.; Litvak, A. M., and Matusoff, I.: Paroxysmal Tachycardia in Children: Report of Four Cases and One Postmortem Examination, Am. J. Dis. Child. **43**:93 (Jan.) 1932. (*c*) Barker, P. S.; Wilson, F. N.; Johnston, F. D., and Wishart, S. W.: Auricular Paroxysmal Tachycardia with Auriculoventricular Block, Am. Heart J. **25**:765 (June) 1943.

2. Decherd, G. M., Jr., and Herrmann, G. R.: The Association of Paroxysmal Atrial Tachycardia with Atrial Flutter and Fibrillation, Am. Heart J. **28**:457 (Oct.) 1944.

3. Hubbard, J. P.: Paroxysmal Tachycardia and Its Treatment in Young Infants, Am. J. Dis. Child. **61**:687 (April) 1941.

the diagnostic criteria employed by the authors have not always been the same, and some doubt has arisen as to whether all cases should be classified as instances of auricular flutter. In all cases there were certain clinical features in common, however and in all, the manifestations were accompanied with various degrees of block.

Auricular flutter without block was noted in 12 cases reported by Shookhoff, Litvak and Matusoff;[1b] 2 reported by Parkinson and Bedford [4] and in single instances reported by Lewis,[1a] McMillan and Bellet,[5] Farr and Wegman [6] and Dressler and Löwy.[7] These cases together with some of those noted in the following paragraphs have been reviewed by Taran and Jennings.[8]

A summary of the 10 reported cases of auricular flutter with block, including our own, appears in the table. The patient described by Koplik [9] was a boy 10 years of age who suffered from attacks of abdominal pain, vomiting, weakness, dyspnea and enlargement of the liver. The attacks lasted from three minutes to forty-eight hours and occurred at irregular intervals throughout an eighteen month period of observation.

In the child reported by Amberg and Willius [10] auricular flutter developed at the age of 4½ years. The auricular rate was 330 and the ventricular rate 105, with degrees of block varying from 2:1 to 4:1. Treatment with digitalis, merbaphen and ammonium chloride led to auriculoventricular dissociation without restoring a normal rhythm. At autopsy a month later an opening 2.5 cm. in diameter was found in the auricular septum, and the right auricle and pulmonary artery were dilated.

The patient of Poynton and Wyllie [11] was an infant observed from the age of 4 months to 3½ years. Throughout this period of time, he had frequent attacks of dyspnea, cyanosis and symptoms which appeared to be due to abdominal pain. The liver became enlarged during the attacks. The symptoms recurred frequently and lasted about one-half

4. Parkinson, J., and Bedford, D. E.: Course and Treatment of Auricular Flutter, Quart. J. Med. **21**:21 (Oct.) 1927.

5. McMillan, T. M., and Bellet, S.: Auricular Flutter: Some of Its Clinical Manifestations and Its Treatment, Am. J. M. Sc. **184**:33 (July) 1932.

6. Farr, L. E., and Wegman, M. E.: Extreme Tachycardia in the Newborn, Am. J. M. Sc. **190**:22 (July) 1935.

7. Dressler, W., and Löwy, M.: Ueber paroxysmale Tachykardie im Kindesalter, Med. Klin. **22**:1481 (Sept. 24) 1926.

8. Taran, L. M., and Jennings, K. G.: Paroxysmal Atrioventricular Nodal Tachycardia in a Newborn Infant, Am. J. Dis. Child. **54**:557 (Sept.) 1937.

9. Koplik, H.: Paroxysmal Tachycardia in Children, Am. J. M. Sc. **154**: 834 (Dec.) 1917.

10. Amberg, S., and Willius, F. A.: Auricular Flutter with Congenital Heart Disease, Am. J. Dis. Child. **32**:99 (July) 1926.

11. Poynton, F. J., and Wyllie, W. G.: Auricular Flutter in Infancy, Lancet **2**:371 (Aug. 21) 1926.

Summary of Data in Eleven Reported Cases of Auricular Flutter with Block

Author	Age at Onset	Preceding Illness	Severity of Circulatory Symptoms	Auricular Rate	Degree of Block	Duration of Attack	Drug Therapy	Outcome	Period of Observation (After Cessation of Arrhythmia)	Comment
Koplik (1917)	10 yr.	None	Marked	180 to 192	2:1	Frequent attacks for 3 min. to 48 hr. over a period of 1½ yr.	None	Unimproved		
Amberg and Willius (1926)	4½ yr.	Congenital heart disease	Marked	330	2:1 4:1	1 month	Digitalis, ineffective; merbaphen; ammonium chloride	Died	.....	Auricular septal defect (autopsy)
Poynton and Wyllie (1926)	4 mo.	None	Marked	...	2:1 3:1	Frequent attacks for ½ hr. over a period of 3 yr.	Digitalis, ineffective; quinidine, ineffective	Unimproved	.....	Withstood attack of pneumonia during arrhythmia
O'Donovan (1929)	5 yr.	Diphtheria	Mild	330	2:1	2 days	None	Recovered	3 mo.	Paralysis of ocular pharyngeal and leg muscles simultaneously with arrhythmia
Carr and McClure (1931)	Birth	None	Mild	380	2:1 3:1	10 days	None	Recovered	5 mo.	Fetal cardiac rate of 160
Sherman and Schless (1934)	1 mo.	None	Mild	464	2:1	2 months	Digitalis, first course ineffective; second course effective (2 mo. later)	Recovered	1 mo.	Fetal cardiac rate of 190
Campbell (1937)	3 yr.	Bronchitis and otitis media	Marked	260	2:1 3:1	Recurrent over period of 2 mo.	Digitalis, effective	Recovered	2 yr.	
Halbertsma and Hartog (1939)	2 yr.	Pneumonia two months before	Mild	330	2:1	3 years	Digitalis, first course ineffective; second course effective (3 yr later)	Recovered	A few mo.	Withstood several illnesses during arrhythmia
Calo (1939)	4½ mo.	Congenital heart disease and whooping cough	Mild	140 to 150	AV dissociation	Few days	None	Arrhythmia disappeared; died 10 mo. later	3 mo.	Probable ventricular septal defect
Calo (1939)	26 days	Congenital heart disease	Marked	440	2:1 4:1	13 months	None	Died	.....	Cardiac hypertrophy (autopsy)
Hoyer and Lyon (1946)	6 days	Trauma of tissues of the neck at birth	Mild	410	2:1	4 months	Digitalis, ineffective	Recovered	6 mo.	

hour each time. Eating, loud noises of emotional stimuli sometimes initiated the tachycardia. From the electrocardiograms the authors made a diagnosis of auricular flutter with a 2:1 or 3:1 block. A soft systolic murmur could be heard in the apical area. Between attacks the child was entirely well and passed through infections such as pneumonia and tonsillitis without difficulty. Rest in bed, digitalis and quinidine seemed to help check the attacks but did not prevent their recurrence.

In the 5 year old child observed by O'Donovan [12] auricular flutter developed with a 2:1 block approximately five weeks after a diphtheritic infection. Paralysis of ocular, pharyngeal and leg muscles occurred simultaneously with the cardiac irregularity. The flutter persisted for only one or two days.

The infant reported on by Carr and McClure [13] had a fetal heart rate of 160 with some irregularity of rhythm. The mother's health had been good throughout pregnancy except for slight uterine bleeding during the first three months of the gestation period. After birth, the infant's cardiac rate varied from 180 to 192, and there was an arrhythmia accentuated by crying and by deep inspiration. The infant vomited frequently and was slightly cyanotic when he cried. Slight cardiac enlargement was demonstrated in the roentgenograms, and a faint systolic murmur could be heard. The electrocardiogram showed auricular flutter with a 2:1 or 3:1 block. On the tenth day of life the regular rhythm was restored, and it was still normal six months later.

The patient observed by Sherman and Schless [14] had a fetal cardiac rate of 190. The mother's health during pregnancy had been good. No abnormalities of the infant were noted during the first week after birth, and not until he reached an age of 1 month was dyspnea, cyanosis and a tachycardia with a pulse rate of 256 noted. At 6 weeks of age, the infant had a ventricular rate of 232 and an auricular rate of 464, with spells of coughing, pallor, weakness and dyspnea. Roentgenograms showed some cardiac enlargement. Digitalis administered at the age of 1 month was without effect, but when repeated at the age of 3 months it caused a drop in rate to 120 and the disappearance of the arrhythmia and of all symptoms of circulatory failure.

Campbell [15] reported 3 cases of paroxysmal tachycardia in infants and young children, 1 of whom had an auricular flutter with a block. This

12. O'Donovan, P.: Auricular Flutter After Diphtheria in a Child, Lancet **1**:607 (March 23) 1929.

13. Carr, J. G., and McClure, W. B.: Auricular Flutter in a Newly Born Infant, Am. Heart J. **6**:824 (Aug.) 1931.

14. Sherman, J., and Schless, R. A.: Auricular Flutter in a Newborn Infant, J. Pediat. **5**:802 (Dec.) 1934.

15. Campbell, M.: Paroxysmal Tachycardia in Infants, Guy's Hosp. Rep. **87**:205 (April) 1937.

child, 3 years of age, had several attacks of tachycardia following bronchitis and otitis media. Block in degrees of 2:1 or 3:1 were noted on occasions over a period of about two months. Following therapy with digitalis complete recovery occurred, and he remained well for the next two years.

The 2 year old child reported on by Halbertsma and Hartog [16] had a pulse rate of 165 two weeks after an attack of pneumonia. Digitalis (Digalen) given at that time produced an irregularity and a bradycardia of 62 beats per minute. Two months later an electrocardiogram showed an auricular flutter with a 2:1 block. There was slight cardiac enlargement and a systolic murmur in the third left interspace near the sternum. The cardiac condition persisted for three years. Although the child was pale and dyspneic on exertion, he passed through several illnesses without serious effects. When a second course of digitalis (powdered leaf) was administered, the ventricular rate dropped from 160 to 120, a normal rhythm was established and all signs of decompensation disappeared.

Calo [17] observed 2 young infants with congenital heart disease in whom auricular flutter developed. One, aged 4½ months when first seen, had evidence of an interventricular septal defect, and had the arrhythmia with auriculoventricular dissociation for a short period of time following an attack of whooping cough. In the other patient, who had an extremely large heart and who was considered to have an idiopathic cardiac hypertrophy, auricular flutter with various degrees of block developed at 26 days of age, and the condition persisted up to the time of his death, at 14 months.

From this small group of patients it is evident that the condition may occur at any age of childhood. In 2 instances the rapid fetal cardiac rate suggested that the arrhythmia had been present before birth.

No predisposing factors were noted in 4 instances. In the case of the 2 infants with rapid fetal cardiac rates, the mothers had had essentially normal pregnancies. Congenital heart disease occurred in 3 other patients. An auricular septal defect was demonstrated at autopsy in 1 instance and unexplained hypertrophy in another. In the third patient, an interventricular septal defect was suspected from clinical findings alone, and there was the additional factor of pertussis which immediately preceded the attack of arrhythmia. In other patients. diphtheria, pertussis, pneumonia and bronchitis associated with otitis media occurred in single instances. In the patient we observed, the only abnormality was a birth injury of the tissues of the neck.

16. Halbertsma, T. J., and Hartog, H. A. P.: Auricular Flutter in a Young Infant with Recovery on Digitalis Therapy, J. Pediat. **15**:114 (July) 1939.

17. Calo, A.: Deux cas de flutter auriculaire chez des nourrissons porteurs d'une cardiopathie congénitale, Arch. d. mal. du cœur **32**:978 (Nov.-Dec.) 1939.

The symptoms varied greatly. Five of the patients seemed to suffer considerable distress, and dyspnea, cyanosis and acute passive congestion of the abdominal viscera quickly developed. During the attacks, the heart sometimes became enlarged, and soft systolic murmurs were audible. The 4 other patients had only mild symptoms, restricted to slight dyspnea, fatigue and failure of growth to occur at normal rates. This was especially true of the patient reported by Halbertsma and Hartog, who had auricular flutter continuously for three years and who withstood several severe infections during that period. In the patient of Amberg and Willius pneumonia developed during the time when the auricular flutter was present, and he recovered with difficulty.

The only deaths were those of the 3 patients with congenital cardiac disease; hence it is difficult to evaluate the influence of the arrhythmia on the prognosis. Two other patients continued to have attacks of the arrhythmia at the time their histories were reported. The majority of the other children seemed to have recovered completely, although only 1 patient had been observed as long as two years after cessation of the auricular flutter.

Treatment with digitalis was successful in 3 instances and failed in 3. It was interesting to note, however, that not until second courses of the drug had been administered to 2 of the former group of patients did they respond by resuming at once a normal sinus rhythm. The 3 other infants recovered spontaneously without treatment and 1, our own patient, recovered spontaneously two months after digitalis had been administered. It seems reasonable to conclude that some patients with auricular flutter and block will resume a normal cardiac rhythm without therapy, but when the condition is severe or protracted repeated courses of digitalization deserve trial. The fact that digitalis may cause auricular fibrillation or other arrhythmias is illustrated by the case history reported by Halbertsma and Hartog. Close supervision of the patient during the course of therapy is therefore necessary.

SUMMARY

Auricular flutter with auriculoventricular block occurred in an infant shortly after birth and persisted until he was approximately 4 months of age. At that time a normal sinus rhythm was resumed spontaneously, and the infant has remained well for the peroid of six months during which he has been observed. The only possible predisposing factor was an unusual traumatic injury to the tissues of the neck.

Ten previous reports of auricular flutter and block in children have been reviewed.

Abstracts from Current Literature

Biochemistry, Bacteriology, and Pathology

THE INFLUENCE OF STREPTOMYCIN AND STREPTOTHRICIN ON THE INTESTINAL FLORA OF MICE. DOROTHY G. SMITH and HARRY J. ROBINSON, J. Bact. **50**:613 (Dec.) 1945.

The authors have in the present investigation attempted to determine the effect of streptomycin and streptothricin in enteric infections by measuring the effect of these agents on the intestinal flora of mice. The preparations were fed to mice in their diet, and it was found that streptothricin and especially streptomycin produced a rapid and pronounced reduction in the numbers of both the coliform and the non-lactose-fermenting organisms in the feces. The observation was made that the dose of streptothricin required for effective reduction was one-half the toxic dose. However, the dose of streptomycin was much below the toxic dose and maintained the reduced number of organisms as long as therapy was continued. Both drugs produced a distinct change in the intestinal flora but did not appear to stimulate the development of resistance.

STOESSER, Minneapolis.

THE ACTION OF PENICILLIN ON STAPHYLOCOCCUS. R. F. PARKER and HARRIET C. MARSH, J. Bact. **51**:181 (Feb.) 1946.

The statement has been made that bacteria exposed to one of the active members of the sulfonamide group continue to grow at a normal rate for a short period of time. Then growth is interrupted and bacterial death begins. The question has come up whether there is a similar lag in the onset of effective action of penicillin. The studies undertaken by the authors revealed that at low concentrations of penicillin the lethal action of the antibiotic agent on Staphylococcus organisms is preceded by a period of unaffected growth, while at higher concentration the lethal action appears to begin without lag. When the bacterial cells are removed to a penicillin-free medium, the effect of penicillin persists for a time. Staphylococcus organisms exposed to 1 unit of penicillin per cubic centimeter of culture medium continue to die after removal of the penicillin, and after a period of some three hours growth is resumed. At lower concentrations of penicillin, exposure for a comparable time may lead to no deaths, but growth is inhibited for three hours after removal of the drug. These observations should have definite clinical application.

STOESSER, Minneapolis.

Metabolism; Infant Feeding; Milk and Other Foods

THE HIGH NUTRITIVE VALUE OF SKIM MILK. R. C. HUTCHINSON, M. J. Australia **1**:457 (May 5) 1945.

In Australia there is an enormous amount of skim milk available every year, but most of it is used for feeding pigs and calves. The waste from this use is shown by the fact that the return to human use as available food protein is only about 13 to 16 per cent whereas if the milk is used directly as food the utilization is about 98 per cent.

All clinical experiments have shown a definite benefit from the use of skim milk when it is added to the diet of children not receiving milk.

There is such a deep-seated prejudice against the use of skim milk that it would probably be necessary to introduce new products into the dairy markets using names that do not indicate their origin.

TENNEY, Madison, Wis.

A STUDY OF THE PATHOLOGIC ANATOMY OF THE EAR IN ATHREPTIC INFANTS. RAOUL CAUSSÉ, Arch. franç. de pédiat. **3**:26, 1946.

Although the relation of athrepsia to disease of the hearing apparatus has been frequently discussed from a clinical viewpoint the pathologic anatomy of auricular lesions has received only scant attention. At the Laboratory of Experimental Otology in Paris, Caussé has examined 17 petrous bones from 13 infants. Eleven of these infants died of athrepsia, and the ear in most of the cases was involved, as reported by the pediatrician or the otologist. Antrotomy has been performed in 5 cases. Three petrous bones from 2 infants dying of a congenital anomaly and a subphrenic abscess, respectively, served as controls.

Following an exhaustive histologic examination outlined in great detail and profusely illustrated, the author concludes: Section of the petrous bones of those infants who succumbed to athrepsia showed all varieties of otitis from the most benign to severe with involvement of the mastoid and the labyrinth. In the 2 babies who died of a nonauricular disease, minimal lesions of otitis were found, confirming the statement of Wittmaack that, regardless of the clinical history, autopsy reveals significant signs of otitis in 50 to 90 per cent of subjects. The relation of auricular disease to athrepsia is entirely a clinical one and the appearance of the bony structures is not necessarily an index of the general severity of the infection. Since the idea, occasionally expressed in the literature, that athrepsia is always of auricular origin is false, it is obviously irrational to practice antrotomy in all cases. Auricular involvement must be considered as an epiphenomenon only.

AMESSE, Denver.

Vitamins; Avitaminoses

RESEARCH ON METABOLISM OF VITAMIN D.: I. RETENTION AND DISTRIBUTION OF VITAMIN D IN THE TISSUES OF A BABY HAVING RECEIVED 15 MG. OF CALCIFEROL BY INTRAMUSCULAR INJECTION. R. HOUET, Ann. pædiat. **166**:169 (April) 1946.

A small boy aged 4 months, suffering with rickets and bronchopneumonia, died four days after an injection of 15 mg. of vitamin D_2. With colorimetric processes vitamin D was found only in the brain (1,600 micromilligrams), in the kidneys (640 micromilligrams) and in the liver (40 micromilligrams). The muscle into which the vitamin was injected yielded about 3,800 micromilligrams of the vitamin. Other muscles, the heart and the lung, were found totally free of the vitamin.

AUTHOR'S ABSTRACT.

Newborn

THE USE OF RH-POSITIVE BLOOD CELLS IN THE TREATMENT OF ERYTHROBLASTOSIS FETALIS. PETER G. DANIS, JACKSON K. ETO and JOHN S. SENNOTT, J. Pediat. **28**:457 (April) 1946.

The use of Rh-positive blood cells in the treatment of erythroblastosis fetalis is reported to have been satisfactory in a proportionately large group of cases. The authors question the necessity for the use of Rh-negative blood cells. They question in theory the desirableness of giving Rh-negative blood, with consequent exposure of the baby's hemopoietic system to the brunt of the agglutination by the Rh antibody.

This, plus their poor results with the use of Rh-negative blood and the recognition of a large variation in the types of Rh serums, stimulated the authors' study in this regard. They further advocate that the blood cells for erythro-

blastosis fetalis be concentrated, since one is dealing with a hemolytic type of anemia, and that dextrose and choline chloride be used as therapeutic agents against hepatic dysfunction.

AUTHORS' ABSTRACT.

FEVER OF THE NEWBORN INFANT. MAURICE LUST, Arch. franç. de pédiat. **3**:60, 1946.

It is a matter of common observation that the neonatal period may be marked by hyperthermia. Such a rise in temperature may be due to diverse factors, such as environment, infection, cerebrospinal lesions or alimentary upsets.

With the instability of the heat-regulating apparatus, so easily demonstrated in the first few days of life, it is obvious that the temperature of the body will promptly be influenced by excessive heat or heavy clothing. The humidity of the atmosphere may also produce a response as significant as that noted in toxic states.

With the exception only of pemphigus, infections of the newborn are much less frequent than formerly.

The author proceeds to discuss the various types of infection still found in even the best supervised nurseries, with special consideration of pathogenesis and treatment.

AMESSE, Denver.

Acute Contagious Diseases

OBSERVATIONS ON THE EPIDEMIC OF POLIOMYELITIS IN CENTRAL FRANCE IN 1943. P. ROHMER, R. SACREZ and P. KERN, Arch. franç. de pédiat. **3**:50, 1946.

This was the first invasion of infantile paralysis in this region since 1930. On account of conditions prevailing in wartime, certain studies had to be abandoned, but it is believed that valuable data were accumulated and that the stimulus for further research was maintained to a high degree among the medical groups concerned.

Numerous case histories are reported, especially those representing the graver types of the disease. The paper concludes as follows: 1. The epidemic was of particular interest because of the large number of adults affected. 2. The stage of invasion was marked by fever, meningeal symptoms and diffuse pain in the limbs and the back. 3. Atypical forms were frequent. 4. Changes in the spinal fluid paralleled those of preceding epidemics but there was a persistence of hyperalbuminorachia, in some cases continuing for months. 5. Beneficial effects from serum treatment were not verified.

AMESSE, Denver.

DAMAGES OCCURRING IN SMALLPOX VACCINATION IN 1940 IN CANTON OF BERNE. FELIX OESCH, Ann. pædiat. **160**:94 (Jan.-Feb.) 1943.

It is established that injury due to vaccination in the Canton of Berne, Switzerland, is of slight extent. Formerly, it was variously claimed that the rarity of injury due to vaccination in Switzerland is consequent on the individual vaccination. The fact that relatively few Swiss allowed themselves to be vaccinated enabled the vaccinator to make a more exact anamnesis than was possible with mass vaccination in adjacent countries. The carrying out of the 119,989 public vaccinations in the Canton of Berne in a few months certainly compelled our vaccinators to perform so-called mass vaccinations. The relative rarity of complications after vaccination seems to us to be the result of the conscientious work of our vaccinators, who refused to vaccinate any one endangered by infection or ill. The memorandum on preventive vaccination against smallpox issued by the Swiss Federal Health Office, which greatly standardized vaccination technic (not all doctors, we have heard, confined themselves to one vaccination incision but made two; even with this method there were no increased local complications) and warned doctors against vaccinating sick candidates may have contributed to the low number of complications after vaccination.

AUTHOR'S ABSTRACT.

Chronic Infectious Diseases

SULFADIAZINE IN EXPERIMENTAL TUBERCULOSIS. C. RICHARD SMITH and FRANK W. OESCHSLI, Am. Rev. Tuberc. **52**:83 (July) 1945.

In the search for a chemotherapeutic agent against tuberculosis, sulfadiazine recommends itself for trial because of an unusually low toxicity. In this experiment a group of guinea pigs was infected by the subcutaneous injection of 1 cc. of a suspension containing 0.0001 mg. of a moist culture of virulent human tubercle bacilli. Treatment with the drug was started on the same day as the inoculation, following an eight day period of gradual acclimatization to the drug. Sulfadiazine powder was incorporated in the feeding pellets. The average daily intake of the drug was estimated at 257 mg., equal to 524 mg. per kilogram. The experiment was scheduled to run for twenty-eight days. Blood concentrations of free sulfadiazine at the end of twenty-eight days averaged 12.2 mg. per hundred cubic centimeters. At autopsy, twenty-eight days after the beginning of treatment, the treated animals were found to have less tuberculosis than the controls in every case. Three of the treated animals were free of disease grossly and microscopically. The spleens failed to reveal the organism on gross examination in 22 guinea pigs, on gross and microscopic examination in 10 and on cultural examination in 2. The livers gave negative results on gross inspection in 20, on gross and microscopic examination in 14 and on culture in 6. The tracheobronchial lymph nodes failed to reveal the organism microscopically in 12 cases. The numbers of tubercle bacilli cultured from the spleens and livers of the controls were on the average about fourteen times greater than those cultured from the organs of treated animals. The calculated number of grams of tuberculous tissue in the tracheobronchial lymph nodes was on the average 400 times greater in the controls than in the treated animals.

The delayed appearance of sensitivity to tuberculin (to 0.1 cc. of a 5 per cent dilution of old tuberculin) in the treated animals was parallel to the postmortem observations. This suggests that the speed of the evolution of allergy is dependent on the number of tubercle bacilli entering the tissues.

While in this experiment invariable inhibition of the disease was found in a large number of animals, the question still remains as to whether trials of treatment with sulfadiazine on human beings with tuberculosis should be recommended. Compared with other drugs which have been suggested, however, the widespread use of and familiarity with sulfadiazine together with its relative safety and its low proportion of side reactions are in favor of clinical trial.

EUGENE SMITH, Ogden, Utah.

SENSITIVITY OF THE TUBERCULIN PATCH TEST (VOLLMER-LEDERLE): RESULTS WITH THREE HUNDRED AND EIGHTEEN PERSONS PRESENTING VARIOUS DERMATOSES. KURT LOWENTHAL, Arch. Dermat. & Syph. **52**:249 (Oct.) 1945.

The purpose of this report was to compare the degree of sensitivity to the Vollmer patch test with that to the intradermal tuberculin test. The results of the study showed that the patch test is equal in sensitivity to a 1:100,000 dilution of old tuberculin injected intracutaneously. Of the 90 patients who had positive reactions to a 1:10,000 dilution of old tuberculin, 78 had positive reactions to patch tests, and of the 18 patients who had positive reactions to 1:1,000 dilution of old tuberculin, only 6 had positive reactions to patch tests. It was concluded that the patch test does not possess a high degree of sensitivity and is the equal of the Mantoux test only for persons highly sensitive to tuberculin.

McINTOSH, Iowa City.

THE IMPORTANCE OF DETECTING TUBERCULOSIS IN CHILDREN. J. A. MYERS, F. E. HARRINGTON and E. GARCIA SUAREZ, J. A. M. A. **128**:852 (July 21) 1945.

There is no phase of the examination for tuberculosis which provides so much specific and accurate information for so many people as the tuberculin test. The obtaining of positive reactions in children establishes the fact that contagious cases

have been in their environment and that the children have primary lesions containing tubercle bacilli (usually living bacilli) with tissue sensitivity to the tuberculoprotein. A negative reactor does not harbor living bacilli except during the preallergic or preterminal stages of the disease.

Tuberculin testing of children in Minneapolis over the past eighteen years has shown a decrease in the number of reactors. For first testing, 1.0 mg. of tuberculin can now be safely used. Of 512 positive reactors from 6,668 children in 1944, 385 had no known exposure to tuberculosis.

All children with positive reactions should have one roentgenogram of the chest to rule out other thoracic disease and, in children over 12, to discover possible tuberculosis of the reinfection type. Roentgenograms in the absence of a positive cutaneous reaction or of tubercle bacilli in the sputum are not specific. The finding of calcium deposits has no significant meaning. Annual roentgen examinations of the chests of reactors should be made after adolescence to permit the discovery of early reinfection lesions. Routine roentgenograms of the chests of nonreactors are not worth while.

BAIRD, Wauwatosa, Wis.

Diseases of Blood, Heart and Blood Vessels and Spleen

THE ELECTROCARDIOGRAM AND CARDIAC STATE IN ACTIVE SICKLE-CELL ANEMIA. T. WINSOR and G. E. BURCH, Am. Heart J. **29**:685 (June) 1945.

The authors studied the cardiac condition of the patients in 25 clinical cases of active sickle cell anemia, together with the pathologic changes noted at 9 autopsies.

The most significant observation was cardiac enlargement, which was noted in 95 per cent of the cases. Systolic and diastolic murmurs occurred at the aortic, pulmonic and mitral areas. The diagnosis was frequently confused with rheumatic or congenital heart disease. Dyspnea on exertion was a frequent complaint.

The pathologic changes in the cardiac muscle consisted of pronounced interstitial edema and degeneration of the sarcoplasm. Six of the 9 patients examined at autopsy had endarteritis of the pulmonary arterioles.

The electrocardiograms did not reveal any characteristic pattern for patients with heart disease due to sickle cell anemia. The tracings showed definite abnormalities in 16 per cent of the patients, and suggestive changes in 4 per cent. The positive results included a prolonged P-R interval and variations in the T waves.

GIBSON, Chicago.

CONGENITAL HEART DISEASE: CASE REPORTS ON THREE MEMBERS OF A FAMILY. I. STEIN and D. J. BARBER, Am. Heart J. **30**:118 (Aug.) 1945.

The authors report congenital cardiovascular anomalies in a mother and 2 children. The mother had coarctation of the aorta, and the children had patency of the ductus arteriosus. Of further interest was the fact that the mother's sister had 3 sons, 1 of whom died of congenital heart disease at the age of 8 years. Another was rejected by the Air Corps because of a "heart condition," and the third was placed on limited service in the Army because of a "heart condition and high blood pressure."

The infrequency of the occurrence of congenital heart disease in more than one member of a family is pointed out.

GIBSON, Chicago.

PULMONARY STENOSIS WITH INTACT INTERVENTRICULAR SEPTUM: REPORT OF ELEVEN CASES. J. H. CURRENS, T. D. KINNEY and P. D. WHITE, Am. Heart J. **30**:491 (Nov.) 1945.

The authors report 11 cases of stenosis of the pulmonary valve in which the interventricular septum was intact. In 9 the stenosis involved the pulmonary annulus, while in 2 the valve leaflets were chiefly affected.

A systolic murmur was noted in each case, and the intensity of the murmur paralleled the degree of stenosis of the pulmonary valve.

Cyanosis was well marked in 4 cases, while in the remainder it was negligible.

Congestive heart failure was the chief or the contributing cause of death in 5 cases.

Electrocardiograms obtained in 4 cases showed right axis deviation.

Roentgen examination failed to reveal any characteristic configuration, though cardiac enlargement was present.

GIBSON, Chicago.

FATAL MEDITERRANEAN (COOLEY'S) ANEMIA. G. RICHARDA WILLIAMSON and RENA CRAWFORD, New Orleans M. & S. J. **98**:280 (Dec.) 1945.

Fatal Mediterranean (Cooley's) anemia in 3 of 11 siblings is reported. Studies of the phosphorus in the red cells and the plasma of 1 patient showed high total and lipid phosphorus and low ester phosphate in the cells, while the plasma showed low lipid phosphorus and high ester phosphate.

BERKLEY, Beverly Hills, Calif.

ACUTE FEBRILE HEMOLYTIC ANEMIA: REPORT OF A CASE. BINDSCHEDLER, APFFEL and ADRIAN, Arch. franç. de pédiat. **3**:89, 1946.

A boy of 13 years was admitted to the Clinic at Strassburg, April 4, 1939, because of grave anemia. His general condition was so poor that even a hurried examination was followed by syncope. The family history was good, and the patient had been well until a month previous, when he lost his appetite, became pale and complained of headache. For the previous four days the boy had been extremely weak but managed to attend school until two days before admission. His illness was then suddenly accentuated; violent abdominal pain was reported, with vomiting and extreme pallor. The skin had a slight icteric tint, and fever developed.

Examination confirmed these findings. There was a pronounced systolic murmur; the spleen was enlarged and extended 2 fingerbreadths below the costal arch; the entire abdomen was rigid.

The blood picture showed 1,000,000 red blood cells and 14,000 white blood cells, with 90 per cent polymorphonuclear cells, a few nucleated red cells and, in the following days, a limited number of myelocytes.

A transfusion of 150 cc. was immediately given, and a sternal puncture was made to determine the nature of the disease. This showed an extreme degree of hemopoietic activity. At least 8 red cells were found for every 2 in the white series. The condition of the patient became progressively worse. On April 6 the hemoglobin value fell to 20 per cent and the red blood cells to 750,000, with 6 per cent reticulocytes. The boy showed profound mental confusion. Daily transfusions were offered from April 6 to April 12, in amounts varying from 150 o 300 cc. An iron preparation and ascorbic acid were also administered. On April 15 he was still anemic, the spleen was much enlarged and the appetite poor, but from this time there was improvement which continued until his complete restoration in June.

In assembling data for diagnosis in this case it was rational to assume, with the temperature present, that one was dealing with an infectious disease. It was necessary also to eliminate acute leukemia, which was readily done by sternal puncture. The history and clinical picture seemed to conform in every respect to the grave form of acute febrile hemolytic anemia described by Lederer and Brill. The etiology of this disease remains unknown, but drastic treatment often results in recovery.

AMESSE, Denver.

MACROCYTIC (HEMOLYTIC) ANEMIA AND HEPATIC DISEASE. S. VAN CREVELD, Maandschr. v. kindergeneesk. **10**:198 (Feb.) 1941.

A boy 4 years old with transient mild attacks of jaundice had a macrocytic hyperchromic anemia at the last attack. There was no enlargement of the liver and the spleen; results of a galactose tolerance test were abnormal. The anemia soon disappeared during a stay in the clinic without any therapeutic measure. There is an extensive discussion of the differential diagnosis; special attention is

drawn to the occurrence of macrocytic anemia in diseases of the liver. The morbid picture can be explained as an atypical hemolytic jaundice complicated by a disturbance in hepatic function.

AUTHOR'S ABSTRACT.

Diseases of Nose, Throat and Ear

HISTAMINE-LIKE SUBSTANCE PRESENT IN NASAL SECRETIONS OF COMMON COLD AND ALLERGIC RHINITIS. ELIZABETH TROESCHLER-ELAM, GIACOMO R. ANCONA and WILLIAM J. KERR, Am. J. Physiol. **144**:711 (Oct.) 1945.

The presence of a histamine-like substance in the nasal secretions of allergic rhinitis has been reported. In this paper the authors present the results of their investigation of the total amount of histamine extractable from nasal secretions by a special method which they outline. Secretions were obtained from cases of allergic rhinitis and of common cold. It was found that a substance which stimulates guinea pig ileum is present in the extracts of nasal secretions both from the common cold and from allergic rhinitis. This activity has a dose response curve similar to that of histamine and can be measured in the presence of atropine sulfate. The concentration of the histamine-like substance in nasal secretions varies widely both in the common cold and in allergic rhinitis. A correlation between the number of eosinophils and the histamine content in nasal secretions was not apparent.

STOESSER, Minneapolis.

PLASTIC REPAIR FOR PROTRUDING EARS. M. I. BERSON, Eye, Ear, Nose & Throat Monthly **24**:423 (Sept.) 1945.

Berson emphasizes the emotional effect of protruding ears on children. The shape of the ear is fully formed at 5 years of age, and operation thereafter will not interfere with later growth. Protruding ears are usually congenital. The author repositions the ear by constructing an anthelix, which is lacking. This reduces the distance between the concha and the cuticular margin, as well as the angle between the concha and the side of the head, which is normally 30 degrees. The exact position finally desired for the ears is carefully marked on the skin where the ear should rest against the head. This should be done with the patient in the upright position and before the injection of a local anesthetic agent, since this may shrink the skin. The entire anterior and posterior portions of the proposed field are anesthetized with monocaine hydrochloride 1.5 per cent and epinephrine hydrochloride 1 : 100,000. This is introduced with a 2 inch, 22 gage needle between the skin and the cartilage of the ear and is expressed as the needle is withdrawn slowly and under light pressure. The elliptic section of the skin, already marked, is excised with a small scalpel, and an elliptic portion of the underlying cartilage is resected, care being taken that the skin on the anterior surface is not perforated. By beveling the edges of the cartilages to be approximated, an anthelix is formed. If the removal of cartilage results in the formation of folds of skin on the anterior surface of the ear, these can be reduced by wide undermining of the skin. The margins of cartilage are joined by mattress sutures and the skin is approximated with fine interrupted silk sutures. Gauze impregnated with 5 per cent sulfathiazole ointment is applied to the back of the ear, and moist gauze is pressed into the anterior convolutions of the ear. The dressings are kept in place by a firm dressing for seven days, when the sutures are removed.

SELTZER, Philadelphia. [ARCH. OTOLARYNG.]

THE ISOLATION OF HEMOLYTIC STREPTOCOCCI FROM THROAT SWABS: III. THE VALUE OF ENRICHMENT BROTH CONTAINING POTASSIUM TELLURITE AND CRYSTAL VIOLET. ROBERT M. PIKE, J. Bact. **50**:297 (Sept.) 1945.

The author states that in previous reports it was shown that culturing throat swabs from well children in enrichment broth containing sodium azide and crystal violet prior to plating results in a significant increase of the number of cultures

positive for hemolytic streptococci. Since the selective properties of potassium tellurite are similar to those of sodium azide, it seemed desirable to compare the efficiency of these two substances as aids in the isolation of hemolytic streptococci. A study was set up, and it was found that potassium tellurite enrichment broth is an aid in the isolation of hemolytic streptococci from the throats of normal children but shows no advantage over sodium azide broth. Data are presented in this paper which extend previous observations on the value of sodium azide enrichment broth.

STOESSER, Minneapolis.

PSYCHOSOMATIC ASPECTS OF STUTTERING. BERNARD C. MEYER, J. Nerv. & Ment. Dis. **101**:127 (Feb.) 1945.

This paper is based on a study of 116 stutterers at the National Hospital for Speech Disorders supplemented by the study of several additional stutterers from the author's private practice.

Although stuttering occurred nearly ten times as frequently in families of stutterers as in nonstuttering families, the simple mendelian hereditary pattern did not appear clearcut. Imitativeness and other nonhereditary factors could not be ruled out in most of the patients. On the somatic side, many of them showed vasomotor disturbances of the skin, dilated pupils and hyperactivity of the deep tendon reflexes, without evidence of involvement of the pyramidal tract. Generally, however, only a few showed evidence of constitutional inferiority or of organic disease. The physical findings are not characteristic of stutterers alone but are an expression of a state of anxiety.

On the psychiatric level, the stutterer is often a schizoid person in whom the speech defect is only one of the symptoms and, in the author's opinion, a very necessary symptom, in that it may serve as a defense against anxiety.

JAHR, Omaha.

THE PSYCHOSOMATIC APPROACH TO SPEECH DISTURBANCES. EMIL FROESCHELS, J. Speech Disorders **10**:221, 1945.

Psychosomatic approach yields considerable material for the correction of speech disorders. Many of the symptoms of aphasia, congenital deafness, stuttering, dysarthria, and other speech disorders are due to psychic sources. Knowledge of this phenomenon should be helpful in clinical work.

PALMER, Wichita, Kan.

ACUTE SUBMUCOUS LARYNGITIS. OTTO SCHINDLER, Ann. pædiat. **160**:270 (May-June) 1943.

Two children, 1 aged 2 years and 10 months, the other 1 year old, died in a short time with the symptoms of severe asphyxia soon after a slight catarrh of the upper respiratory tract. In both cases the clinical picture was extremely confused. The pathologic-anatomic examination showed occlusion of the lumen of the larynx, due to the acutely swollen mucous membrane. Microscopically there was, in addition to the severe edematous loosening, a purulent infiltration of the submucosa stretching from the pharynx to the larynx, which led to sudden closing of the respiratory tract before the severe infection could affect the organism. The inflammation of the mucous membrane of the nasopharyngeal cavity is supposed to be the origin, since no other source of infection could be found. Bacteriologically staphylococci and streptococci were found.

AUTHOR'S ABSTRACT.

Diseases of Lungs, Pleura and Mediastinum

MAGNETIC REMOVAL OF FOREIGN BODIES FROM THE FOOD AND AIR PASSAGES UNDER FLUOROSCOPIC GUIDANCE. MURDOCK EQUEN, South. M. J. **38**:245 (April) 1945.

Permanent magnets are now available. The most powerful is known as "cast alnico V" ("alnico" is composed of aluminum, nickle, cobalt and iron). From this

metal, "alnico," two types of magnets have been constructed. One is for use in the tracheobronchial tree through the bronchoscope under fluoroscopic guidance. The other is for use in the esophagus and stomach and is attached to the end of a Levin tube. The tube is passed into the stomach under fluoroscopic guidance. The stomach may be inflated through the Levin tube. A case report is presented in which a metal safety pin was removed from the stomach of a 2 year old child.

LOGAN, Rochester, Minn.

TREATMENT OF CONNECTING PNEUMOTHORAX IN A SMALL CHILD BY MEANS OF PLURAL IRRITATION. JEAN LOUIS BURCKHARDT, Ann. pædiat. **159**:337 (Dec.) 1942.

The various methods employed in the treatment of spontaneous pneumothorax and pneumothorax with valvular opening are discussed, and closed treatment with slightly positive pressure is recommended.

The author describes a case of pneumothorax with valvular opening after empyema in a small child whom he treated. An intrapleural injection of 30 per cent dextrose solution with purified talc caused the lung to expand completely after atelectasis had existed for at least six months with considerable displacement of the mediastinum.

AUTHOR'S ABSTRACT.

A CASE OF POSTOPERATIVE MASS PULMONARY COLLAPSE IN CHILDHOOD. JEAN MURY and HUBERT MARTIN, Ann. pædiat. **160**:287 (May-June) 1943.

The case of an 8½ year old boy who had collapse of the lung after transcrotal orchidopexy is used for discussion of postoperative pulmonary collapse. This is a rare complication in childhood. The importance of an allergic factor is emphasized. Characteristics of this were found in the appearance of a Loeffler infiltrate some months before the operation and of asthma in a brother.

AUTHOR'S ABSTRACT.

SUPERIOR MEDIASTINALIS PLEURITIS IN THE SMALL CHILD. GABY HARTMANN-STEHELIN, Ann. pædiat. **164**:182 (April) 1945.

Pleurisy of the superior mediastinum in the case of nursing and small children is described by the author. Seventeen such cases are considered; the differential diagnosis and the relationship of the condition to tuberculosis are investigated. Tuberculosis as an etiologic factor stands in the foreground; other causes are rare.

Our observation proved that in 13 cases with certainty the cause was tuberculosis; in the others pertussis played a certain role.

Striking was the fact that the reaction to tuberculin became positive only after long delay. The fact that this reaction is negative one or more times does not exclude the possibility of tuberculosis; one excludes this causation only after an observation period of months and after continuous negative reactions.

The most important differential diagnosis for the nursing child is that from hypertrophy of the thymus. However, the roentgen picture allows with certainty a differential diagnosis.

AUTHOR'S ABSTRACT.

Nervous Diseases

ISOLATION OF ST. LOUIS ENCEPHALITIS VIRUS FROM THE PERIPHERAL BLOOD OF A HUMAN SUBJECT. RUSSELL J. BLATTNER and FLORENCE M. HEYS, J. Pediat. **28**:401 (April) 1946.

A filtrable virus has been isolated from the blood of a patient whose clinical manifestations were suggestive of a virus infection with minimal involvement of the central nervous system. The infectious agent isolated is neutralized by serum of a rabbit immunized to a known strain (Hubbard) of St. Louis encephalitis virus. During the clinical course increasing titer of antibody to the newly isolated

virus and to known St. Louis encephalitis virus (Hubbard) developed in the patient.

The two criteria for the diagnosis of a virus disease have been satisfied: namely, isolation of an infectious agent from the patient and development during the course of clinical illness of type-specific humoral antibodies.

This work represents the first instance of the isolation of the St. Louis encephalitis virus from a human subject during life. It is the fourth instance in which the St. Louis virus has been isolated from natural sources, the first being the initial isolation from tissue taken from the human brain at autopsy, the second from mosquitoes collected in nature during an epidemic and the third from the bodies of chicken mites collected in nature during a nonepidemic period.

The method employed, intraperitoneal injection into young mice with relatively large inoculums, may prove generally applicable for the isolation of virus, especially for the detection of small amounts.

AUTHORS' ABSTRACT.

APPRAISAL OF TREATMENT OF HEMOPHILUS INFLUENZAE TYPE B MENINGITIS WITH SPECIFIC RABBIT SERUM AND SULFONAMIDES. ALBERT M. EDMONDS and ERWIN NETER, J. Pediat. **28**:462 (April) 1946.

Sixty cases of Hemophilus influenzae type B meningitis in infants and children treated with Alexander's type-specific rabbit serum and with sulfonamide compounds were analyzed. These cases were divided into two groups: Group I is comprised of all cases up to Oct. 1, 1944, and group II from Oct. 1, 1944, to May 31, 1945. The following data were obtained: Bacteremia was present in 39 out of 50 cases (78 per cent). The case fatality rate was 33.3 per cent for the entire series, 38.7 per cent for group I and 18.7 per cent for group II. Of the 60 patients, 32 had completely recovered at the time of discharge from the hospital. There was no appreciable difference between the two groups in the rate of complete recoveries. The following complications and sequelae were encountered: purulent arthritis, facial paralysis, partial and complete deafness, foot drop and hydrocephalus associated with mental retardation. The total amount of intravenously injected serum was not the sole factor responsible for the outcome of the disease. Of particular significance is the fact that 8 out of 26 patients succumbed in spite of the administration of more than 200 mg. of antibody nitrogen, including 3 out of 7 patients who received more than 300 mg. All 4 patients who received serum intrathecally at a time when many micro-organisms and a correspondingly large amount of specific soluble substance were present in the spinal fluid succumbed to the infection. The possible deleterious effects of this therapy have been discussed. Intrathecal injection of serum in patients whose spinal fluid contained but a small number of micro-organisms or none at all was followed by clinical improvement and sterilization of the spinal fluid in several instances. The possibility that this form of therapy may have been responsible, in part at least, for the development of hydrocephalus in 2 patients has been considered. Immediate reactions to the type-specific serum injected intravenously were encountered in 7 instances, and delayed reactions in 8. Intrathecal injection of serum resulted in convulsions in 2 patients and fever in 1. Two cases presenting respectively the initial stage and the classical picture of Waterhouse-Friderichsen syndrome, as seen on postmortem examination, were included in the study.

AUTHORS' ABSTRACT.

PENICILLIN AS AN ADJUNCT TO SURGERY IN THE TREATMENT OF BRAIN ABSCESS. LEONARD T. FURLOW, South. M. J. **38**:312 (May) 1945.

The author reports on 6 patients, 1 of them a 3½ year old boy, who was treated by a combination of surgical drainage and intramuscular administration of penicillin. One of the adults died. Emphasis is laid on the fact that the use of penicillin is an adjunct to surgical treatment and not a substitute for it. Intrathecal administration of penicillin is seldom used in the author's hospital, since the agent has been found in the spinal fluid of patients having meningitis who are receiving penicillin intramuscularly.

LOGAN, Rochester, Minn.

ON THE TREATMENT OF INFLUENZAL MENINGITIS BY SULFONAMIDE PREPARATIONS. E. JACOBSSON, Ann. pædiat. **166**:57 (Feb.) 1946.

Thirty-seven patients with influenzal meningitis have been treated at the Children's Hospital in Göteborg, Sweden, since 1924. Nine patients have lived. With one exception the latter were treated with sulfonamide preparations. Among those who died, 9 were treated without success with the usual dosage for the treatment of pneumonia. Patients who were treated and lived were of the following ages: 8, 10, 12½, 5, 4, 2½, and 1 year. Those who died in spite of treatment were less than 15 months (3 were around 1 year of age and the others 6 months or less). The doses have been increased notably in proportion to those which were used for the treatment of pneumonia.

Since 1940, 11 patients have been so treated, 6 of whom have recovered, 2 of whom were less than 1 year of age. The last three or four years determinations of concentration in the blood and cerebrospinal fluid have been made. In patients who lived there was an elevated amount of sulfonamide compounds in the blood and cerebrospinal fluid. In those who died, the amount of sulfonamide compounds was also a little higher during the period of improvement.

Sulfadiazine proved to be the best preparation. It is absorbed easily and completely, but it is eliminated slowly in such a way that an increased amount can be kept in the blood and in the tissues by continuous administration. The secondary toxic reactions (nausea and exanthem) were rare. The danger of lesions of the kidneys or of the blood was slight. The amount in the blood ought never to fall below 12 to 15 mg. per hundred cubic centimeters; that in the cerebrospinal fluid should not fall much lower. One should give doses of four to five times as much in these cases as in cases of pneumonia, usually 0.075 to 0.1 per kilogram (at the beginning a double amount at least twice) at intervals of four hours. Treatment should cease only when a decisive change has occurred and when the number of cells in the cerebrospinal fluid is almost normal, as well as the number of white cells in the blood, the temperature and the sedimentation rate.

AUTHOR'S ABSTRACT.

Psychology and Psychiatry

ANALYTICAL STUDY OF ONE HUNDRED CASES OF ONYCHOPHAGIA (NAIL BITING) IN THE CHILD. M. SCHACHTER and MLLE. S. COTTE, Ann. pædiat. **166**:99 (Feb.) 1946.

The analysis of nail biting in childhood gave the following results:

The history revealed early convulsions in 12 per cent and enuresis in 20 per cent. Mentally, 37 per cent were normal while 34 per cent showed a slight and 26 per cent a severe degree of defectiveness. Among the emotional characteristics attacks of temper were prevalent (31 per cent). Only the full knowledge of the personality and of the children's surrounding enables one to find the best therapeutic solution of so complex a problem as onychophagia.

AUTHORS' ABSTRACT.

Diseases of the Genitourinary Tract

PENICILLIN IN ACUTE NEPHRITIS IN CHILDREN. SUSANTA SEN, Am. J. M. Sc. **211**:289 (March) 1946.

Twelve children with acute nephritis of a severe type were treated with penicillin. There was 1 death after two days of treatment; the results were satisfactory in the other 11 patients. The bactericidal action of penicillin is employed to eliminate the causal infective focus. Results, as judged by the rapid amelioration of signs and symptoms, are encouraging, and a wider trial is recommended.

HENSKE, Omaha.

THE INFLUENCE OF SULFANILAMIDE THERAPY UPON THE COURSE OF ACUTE GLOMERULONEPHRITIS IN CHILDREN. MILTON RAPOPORT, MITCHELL I. RUBIN and ARTHUR D. WALTZ, Am. J. M. Sc. **211**:307 (March) 1946.

A group of 33 children with acute glomerulonephritis treated with sulfanilamide was compared to a group of 40 children with the same disease who were not given this drug. Both groups were comparable in age, sex, duration of illness prior to hospitalization, severity of renal disturbance, incidence of accompanying cardiovascular derangements and predominant infecting organism (the beta hemolytic streptococcus).

All children in both groups recovered completely from their renal disease.

There was no significant difference in the duration of the renal inflammatory process as estimated by routine urinalysis, Addis urinary sediment count and red blood cell sedimentation rate.

There were no statistically significant differences between the duration of the disturbed renal or cardiovascular functions in the two groups.

Sulfanilamide had no demonstrable deleterious effect on the renal function and did not cause an unusual incidence of toxic phenomena in patients with acute glomerulonephritis.

Sulfanilamide therapy appears to be without influence on the course and duration of acute glomerulonephritis in childhood. This does not deny the value of sulfanilamide (and other sulfonamide compounds) in the treatment of infection in the patient with nephritis.

HENSKE, Omaha.

BISMUTH NEPHROSIS WITH ANURIA IN AN INFANT. DAN P. BOYETTE, J. Pediat. **28**:493 (April) 1946.

Reports of the toxic effects of bismuth are not new, and anuria as a symptom of bismuth toxicity is not uncommon, but death due to complete failure of renal function following the administration of a small amount of a bismuth compound to an infant is rare enough to merit mention. The pharmacologic action of bismuth is similar to that of mercury, but the untoward reactions are less frequent and are usually of a less serious nature, the more commonly noted being stomatitis, gastroenteritis, nephrosis and involvement of the central nervous system. As bismuth is excreted mainly in the urine it is more toxic to the kidney than to any other organ.

The case reported was of a 2 year old, 20 pound (9,071 Gm.) infant who received a single intramuscular injection of Thio-Bismol (a dosage of approximately 10 mg. of metallic bismuth) in the treatment of Vincent's gingivostomatitis. Within twenty-four hours the child had ceased to void, and she was admitted to the hospital after thirty-six hours of anuria. The blood nonprotein nitrogen on admission was 76 mg. per hundred cubic centimeters. Intravenous administration of fluids, hypertonic solution of dextrose and theophylline ethylenediamine did not produce diuresis. On the fifth hospital day, as nitrogenous retention in the blood was increasing and in view of the seriousness of the situation, decapsulation of the kidneys was performed with the patient under ether anesthesia. The blood nonprotein nitrogen rose to 123 mg. per hundred cubic centimeters. On the fourth postoperative day transfusions were begun, and concurrently with this therapy the infant began voiding. During the following two days the blood nonprotein nitrogen dropped to 61 mg. per hundred cubic centimeters, and the patient was greatly improved. However, on the evening of the tenth hospital day a generalized erythematous, petechial, macular rash of increased capillary fragility developed; the child presented the picture of one in peripheral vascular collapse and died the following morning in spite of all supportive measures.

Postmortem examination revealed pronounced tubular degeneration (necrotizing nephrosis) throughout both kidneys, and chemical analysis of the renal tissue revealed the presence of 0.5 mg. of bismuth (5 per cent of the original amount) fourteen days after the injection and five days after restoration of renal function.

It is felt advisable to warn of the hazards of administering bismuth compounds to infants by reporting this case. Nephrosis, if it occurs, is best treated by the

intravenous administration of fluids and hypertonic dextrose solution. Whole blood and plasma should be used as indicated. Vasodilators, such as caffeine, theophylline ethylenediamine or theobromine, may be tried without causing further damage. Surgical procedures should be used only as a last resort.

AUTHOR'S ABSTRACT.

PYURIA. ANTONIO LAGUARIBA, J. de pediat. **9**:36 (April) 1943.

Etiologic Factors.—These are lack of vitamins and poor living conditions (secondary to infections of the gastrointestinal and respiratory tracts). The disease is influenced by the season, being more frequent in summer. This all adds up to a lack of resistance.

Pathogenic Factors.—These factors are: (1) disturbances of the water-colloid equilibrium due to dehydration, lowering the resistance of the body and (2) development of germs as a consequence of poor drainage of the urinary tract.

Bacteriology.—Coliform organisms are the most frequently found germs, but germs vary greatly. The ports of entry are the urinary tract or the blood or lymphatic systems.

Clinical Signs.—These are fever, backache, polyuria, enuresis and turbid or bloody urine. The existence of 10 to 15 leukocytes per field is not enough to confirm the pyuria. Etiology is determined by the type of bacteria.

Prognosis.—This is good for acute infections. With chronic infections, the cure takes years.

Treatment.—The methods of treatment are rest, enemas, giving of fluids by mouth, and administration of vitamins, antipyretics and acidifying substances, such as sodium phosphate, benzoic acid and syrup of ammonium mandelate. Methenamine can be given, from 1 to 2 Gm. Treatment with sulfonamide compounds is useful in almost all cases; also lavage of the bladder with boric acid can be done.

LOZOYA, México D. F., Mexico.

Diseases of the Muscles, Bones, Joints and Lymph Glands

VERTEBRAL HEMANGIOMA IN CHILDREN. IRA I. KAPLAN, J. Pediat. **28**:498 (April) 1946.

The usual hemangioma seen in children referred for irradiation is the superficial lesion or birthmark on the skin. Hemangiomas are congenital, to quote Ewing, "of early development, slow in growth and benign in course." Such as appear on the face are most readily recognized and usually attended to early for cosmetic reasons. The less common hemangioma is that involving bone, the symptoms of which resemble various other conditions, and only the roentgenologic examination suggests a hemangioma by reason of the characteristic striated effect. The child usually complains of pain in the back and gradually exhibits signs of functional disturbances of the limbs. During the past two decades there were but 5 cases of bone hemangioma referred for treatment to the Radiation Therapy Department at Bellevue Hospital, and only 1 case of a child with vertebral involvement.

The following case is one of angioma of the vertebrae: E. L., a boy, white, aged 12½ years, was admitted Oct. 2, 1943, complaining of inability to move the legs. A roentgenogram showed hemangioma of vertebrae, and biopsy confirmed the diagnosis. Roentgen therapy with high voltage was instituted, and remarkable improvement resulted. At present the boy is well, up and about, carrying on as any normal child of his age does.

The number of verified cases of bone hemangioma is small. In most instances their finding is incidental to examination following trauma or in cases involving the spine when neurologic symptoms demand attention. The roentgenogram shows a characteristic soap bubble effect. In cases of hemangioma of the vertebrae, if diagnosis is made before irreparable damage to the cord has taken place, irradiation may be expected to effect a cure.

Hemangioma of bone is not common. It frequently involves the spine. Irradiation is the method of choice. Surgical intervention is required in some cases to relieve pressure on the cord.

AUTHOR'S ABSTRACT.

Diseases of the Eye

JUVENILE DISCIFORM DEGENERATION OF THE MACULA. H. LUCIC, Am. J. Ophth. **28**:965 (Sept.) 1945.

Lucic reports his observations in 10 cases of juvenile disciform degeneration of the macula, including the results of microscopic examination in a case in which the condition was mistaken for a tumor. He suggests that the senile and juvenile forms are merely different degrees of the same disease.

W. S. REESE. [ARCH. OPHTH.]

BILATERAL PARTIAL ECTASIA OF THE NERVE HEAD WITH PERIPAPILLARY ECTASIA. I. S. MACGREGOR, Brit. J. Ophth. **28**:618 (Dec.) 1944.

The case described is one of partial ectasia of both optic disks with complete peripapillary ectasia. The disks were not completely excavated. The picture is remarkably similar to the late results of traumatic avulsion of the optic nerve with preservation of the continuity of the vessels except that glial proliferation at the nerve head is usually pronounced in cases of proved avulsion. The condition is regarded as a congenital anomaly of the optic disk. It may be a rare form of birth injury resulting in partial avulsion of the optic nerve rather than a development failure at the disk.

The article is illustrated.

W. ZENTMAYER. [ARCH. OPHTH.]

THE SOCIAL AND MEDICAL PROBLEMS OF PHLYCTENULAR DISEASE IN DUBLIN. J. B. MCAREVEY, Irish J. M. Sc., July 1944, p. 201.

The object of the inquiry was to determine the trend of phlyctenular disease in Dublin, the age and sex incidence, the seasonal incidence, the types of the disease and the occupation of parents of children suffering from the disease. The information was obtained from an analysis of 2,470 new cases at the Royal Victoria Eye and Ear Hospital, Dublin. The periods selected represent World War I, the present war and a normal period immediately before the present war. The study warrants the conclusion that basically phlyctenular disease is a manifestation of malnutrition. It is a disease of the poorer classes, in whose diet the essential proteins necessary to growth and normal development are practically absent, the only source of these substances available to most of the children being milk, in limited quantities; as a result, they suffer from a low grade malnutritional anemia, with a deficiency of some essential vitamins.

It is interesting to note that the evidence of tuberculous infection was positive. 1. The reaction to the tuberculin test was positive in 85.9 per cent of children (13 per cent of controls). 2. Roentgenograms of the chest showed positive evidence in 37.3 per cent of children (20 per cent of controls). 3. There was a history of contact in 5.5 per cent (and of possible contact in 2.9 per cent). 4. The incidence of sanatorium care was 11.8 per cent. The nature of the tissue reaction points to an allergic response.

W. ZENTMAYER. [ARCH. OPHTH.]

RECURRENT GLIOMA OF THE RETINA TREATED BY CHAOUL'S METHOD OF ROENTGEN IRRADIATION. C. COSTA, Arch. Soc. oftal. hispano-am. **4**:72 (Jan.-Feb.) 1944.

The left eye of a boy 1 year old was enucleated for a glioma. Five months later the tumor recurred in the orbit. Treatment was with irradiation according to the method of Chaoul. This technic is considered better than the ordinary method of roentgen irradiation. One month later the tumor had disappeared entirely. Three months later, however, the growth reappeared. The child is still under treatment.

H. F. CARRASQUILLO. [ARCH. OPHTH.]

DERMAL LIPOMA OF THE CONJUNCTIVA WITH SCLERAL CYST AND COLOBOMA OF THE PALPEBRAL ANGLE. W. B. MATTOS, Arq. brasil. de oftal. **5**:39 (April) 1942.

The author presents a clinical observation on a patient 7 years of age. Examination showed a greatly widened palpebral fissure, due to a coloboma of the external angle. In the latter region a large, yellowish rose tumor covered more than half the cornea and extended into the outer portion of the upper and lower cul-de-sacs, preventing the patient from closing the eye. The eye was turned inward, and its movements were much reduced.

Operation was performed, with subconjunctival ablation of the tumor. The conjunctiva was spared as much as possible, the tumor being disinserted from the cornea, to which it was closely adherent. The tumor was dissected along its whole length between the superior, internal and inferior rectus muscles. In the region of the inferior rectus, a scleral cyst was found at 5 o'clock, just behind the limbus. This was not removed but was left for a future operation. As strabismus was present, tenotomy of the internal rectus muscle was performed. At a second operation the scleral cyst was removed and the palpebral coloboma closed. A slight convergent strabismus and a leukoma over one-half the cornea remained.

The author was unable to find any reference in the literature on epibulbar tumors associated with scleral cyst.

M. E. ALVARO. [ARCH. OPHTH.]

CONGENITAL ANIRIDIA: REPORT OF A CASE. H. MARBACK, Arq. brasil. de oftal. **5**:97 (June) 1942.

The author presents a case history.

A man aged 20, with no family history of any ocular defect, showed horizontal nystagmus, which increased involuntarily in a strong light or when the patient tried to fixate objects in distant or near vision. There was complete absence of the iris in both eyes, resulting in an excessively large pupillary orifice, the limit of which was determined by the contour of the cornea, which was of normal size. The cornea was transparent, except in the lower limbal region, where there was a partial embryotoxon. The lens was semidislocated and rotated upward and backward, completely opacified and of a grayish white color. The fundus was normal. In each eye visual acuity taken with a + 13 D sphere was limited to counting fingers at 3 meters. This acuity was relatively good for a case of this kind and in accord with the normal aspect of the fundus, as in the great majority of cases aniridia is associated with absence of the macula.

The author agrees with Duke-Elder that two different mechanisms may produce the same anomaly. 1. Aniridia may result from lack of development of the retinal ectoderm at the level of the edge of the optic vesicle. That aniridia is always associated with other ectodermal defects supports this theory. 2. The anomaly may be the result of a malformation of the vascular mesoderm, due to a mechanical obstruction in the development of the iris, caused by remnants of the fibrovascular capsule of the lens.

M. E. ALVARO. [ARCH. OPHTH.]

Skin Diseases; Allergy

THE ERYTHEMAL THRESHOLD FOR SUNBURN. HAROLD F. BLUM and WILLIAM S. TERUS, Am. J. Physiol. **146**:107 (April) 1946.

The authors describe measurements of erythemal thresholds to ultraviolet radiation under various conditions. The threshold of a given subject varies considerably from time to time. Such factors as sweating and wetting of the skin with water were found to have little effect on the threshold. The paper should be consulted for details, for an analysis of the factors determining the threshold is presented. This analysis shows the inherent limitations of a "standard" erythema spectrum as used to predict the relative sensitivity of a subject to different kinds of polychromatic radiation, and the pitfalls to be encountered in its use.

STOESSER, Minneapolis.

EVALUATION OF PROTECTIVE MEASURES AGAINST SUNBURN. HAROLD F. BLUM, MAYNARD EICHER and WILLIAM S. TERUS, Am. J. Physiol. **146**:118 (April) 1946.

This paper presents the studies undertaken to determine the degree of protection against sunburn afforded by various preventive preparations with the primary aim of selecting those most effective for use under severe conditions. It was found that the degree of protection afforded against sunlight or other polychromatic radiation by a sunburn preventive is a function of a number of variables, including the spectral distribution of the radiation, the transmission spectrum of the preventive and the numerous factors affecting the threshold of the subject. Wide differences in the estimation of the protection afforded by sunburn preventives are obtained by different methods and may lead to erroneous conclusions. The authors summarize by stating that individual estimates of the value of preventives may be widely divergent.

STOESSER, Minneapolis

DERMATITIS OF INFANTS. PIERRE WORINGER, Arch. franç. de pédiat. **3**:40, 1946.

Together with eczema, dermatitis in infants typifies the most widespread form of dermatosis found in early life. Both diseases are peculiar to this period and, in the forms under discussion, have usually been considered similar expressions of individual diathesis. It is commonly recognized, however, that they may now be distinguished clinically and also from the viewpoint of etiopathology; in turn the prognosis and treatment will be radically different.

Dermatologic literature is filled with numerous conceptions of the pathogenesis of dermatitis in young subjects. We find the discussions ranging from seborrheic eczema, parakeratosis psoriasiformis, erythema of the newborn and intertrigo to Leiner-Moussous disease. The simple term "dermatitis" seems most suitable inasmuch as it permits consideration without prior commitment on etiology.

The author follows with the most exhaustive inquiry into the nature of the lesions, the causation, the site of predilection, the evolution of the disease, the differential diagnosis, the pathogenesis, the prophylaxis and the treatment.

In the summary, it is especially stressed that the diagnosis must be based on the mode of onset, the appearance and distribution of the eruptive lesions and their evolution.

AMESSE, Denver.

ACUTE DERMATOMYOSITIS IN THE CHILD. CHARLES WEINBERG-HEYROUTI and L. REIF, Ann. pædiat. **166**:193 (April) 1946.

A case of acute polymyositis in a boy of 4½ years is reported. Extensive edema over the head, the nape of the neck, the back and the extremities with erythema, sweats, muscular pains, impaired function and changed personality characterized this case as dermatomyositis. Cure without any atrophy ensued after six weeks. The only sequel to the illness was slight paresis of the left leg.

The patient's illness differed from the description found in the literature in some points: (1) the exceedingly pronounced hard edema of the face, the scalp, the neck and the lower extremities which pitted deeply on pressure; (2) the existence of a large splenic tumor from the start of the illness and the improvement in the child's health after tonsillectomy, findings which might point to the infectious origin of the illness, and (3) the peculiar psychologic behavior of the patient, who during the height of the illness gave the impression of a badly mentally defective, apathetic and negativistic child.

AUTHORS' ABSTRACT.

Surgery and Orthopedics

BLOOD HISTAMINE LEVELS IN EXPERIMENTAL BURNS. VIVIAN G. BEHRMANN, VICTOR SCHELLING and F. W. HARTMAN, Am. J. Physiol. **145**:483 (Feb.) 1946.

Complications associated with burns of the skin have always been of great clinical interest. In this paper the authors observed an increase in blood histamine

in 13 of 14 of their experimental animals who were burned over 50 to 60 per cent of their body surface and dressed with sterile petrolatum. The blood histamine level rose to two and one-half times the average normal figure within twenty-four to forty-eight hours after the burn, with a maximum approximately five times the normal figure about the fourth day. After the sixth to seventh day the level decreased gradually toward the normal. No positive evidence that the elevated blood histamine levels stimulate excessive gastric acidity or play a role in the formation of Curling's ulcer was noted. The normal or subnormal titrations of gastric acidity which the writers obtained suggest that the blood histamine either was not elevated enough to produce hyperacidity or was in an inactive form.

Daily injections of penicillin in 5 of the animals had no effect on the rising blood histamine values. However, since ulceration did not develop in penicillin-treated animals in spite of elevated blood histamine values, there is further indication that blood histamine does not enter into the pathogenesis of Curling's ulcer.

STOESSER, Minneapolis.

Miscellaneous

A BROTH DILUTION METHOD OF ASSAYING STREPTOTHRICIN AND STREPTOMYCIN. RICHARD DONOVICK, DOROTHY HAMRE, FREDERICK KAVANAGH and GEOFFREY RAKE, J. Bact. **50**:623 (Dec.) 1945.

The authors describe a broth dilution method of assaying streptothricin and streptomycin which is apparently more sensitive and somewhat more accurate than the procedures described heretofore for the assay of these substances. Although the test has only a threefold range, it has the advantage that as little as 0.05 unit per cubic centimeter of these antibiotics will inhibit Klebsiella pneumoniae under the test conditions; thus, with allowance for the volumes added, 1 unit per cubic centimeter of the original solution of either substance can be measured.

STOESSER, Minneapolis.

THE COMBINED ACTION OF PENICILLIN AND THE SULFONAMIDES IN VITRO: THE NATURE OF THE REACTION. MORTON KLEIN and SEYMOUR S. KALTER, J. Bact. **51**:95 (Jan.) 1946.

The combined action of penicillin and the sulfonamide compounds against bacteria has now been the subject of a considerable number of investigations. In this paper the authors tested ten sulfonamide-resistant and sulfonamide-susceptible strains of Staphylococcus aureus and eight gram-negative rods for their susceptibility to the combined action of penicillin and sulfonamide compounds. They found that in vitro combination of sulfathiazole, sulfadiazine or sulfapyrazine and penicillin resulted in an increase in the penicillin titer only if both agents were present in inhibitory concentrations. Also observed was a pronounced delay in penicillin activity when this preparation was added to a bacterial culture five hours after the sulfathiazole. No other in vitro evidence of antagonism between the sulfonamide compounds and penicillin was noted. It appears that the penicillin reduces the total number of bacterial cells to limits within which the sulfonamide compound becomes completely inhibitory.

STOESSER, Minneapolis.

BACILLIN, A NEW ANTIBIOTIC SUBSTANCE FROM A SOIL ISOLATE OF BACILLUS SUBTILIS. JACKSON W. FOSTER and H. BOYD WOODRUFF, J. Bact. **51**:363 (March) 1946.

The authors have obtained a new antibiotic called "bacillin" from a soil isolate of Bacillus subtilis. The substance is highly active against gram-negative and gram-positive bacteria in certain mediums. Described in this paper is the differentiation from known antibiotics, from similar bacteria, the conditions relating to its production in solid and in liquid mediums, the procedure of purification for obtaining highly potent concentrates and some chemical properties. It is found

that crude concentrates of bacillin are moderately toxic for mice and completely ineffective in protecting the animals from virulent bacterial infections. The presence in the medium of blood and other complex natural materials reduces or abolishes the antibacterial properties of bacillin.

STOESSER, Minneapolis.

PROBLEMS OF ADOLESCENCE IN WAR. E. T. HILLIARD, M. J. Australia **1**:249 (March 10) 1945.

The characteristics of adolescence that make the difficulties in adjustment between adult and adolescent points of view are self consciousness or shyness, reticence, moodiness, intellectuality and claims to independence. The adult must recognize these factors and treat them with respect or he may build a barrier between himself and the adolescent.

The two problems of paramount importance that the adolescent must deal with are: (1) the necessity of adjustment to the urgency of the sex drive and (2) the necessity of freeing himself from the family circle. The dislocations of family life in wartime make these adjustments more difficult than ever.

In all child guidance work the almost universal factor in dealing with delinquency was lack of parenteral affection. This makes adult education of great importance, but it is seldom that adults needing this type of education can be induced to accept it.

TENNEY, Madison, Wis.

ASPIRATION BIOPSY. T. E. WILSON, M. J. Australia **1**:268 (March 17) 1945.

The author describes and discusses aspiration biopsy. This procedure, he believes, is of value in distinguishing between inflammatory lesions, cysts and innocent or malignant tumors. It is rarely possible, however, to determine the nature of a malignant tumor by this means. This examination is particularly useful for patients who refuse to submit to removal of specimens by surgical means when repeated biopsies are required for academic purposes, for the biopsy of otherwise inaccessible tumors, for determining the presence and the extent of metastases in the regional lymph nodes prior to operation, for confirming irrefutably the diagnosis of cancer in cases in which treatment of patients by irradiation is to be given and in which cures may later be claimed and for the biopsy of lesions which are particularly prone to fungate after incision. A complete bibliography of the subject is appended.

GONCE, Madison, Wis.

LEAD INTOXICATION IN AN INFANT. B. H. HESSELMAN, Svenska läk.-tidning. **39**:1102 (April 24) 1942.

Lead intoxication in children is a rare disease in Sweden. Hesselman reports such a case. A breast-fed infant began to suffer from vomiting when 3 months old. He was admitted to a children's hospital after three weeks of illness. There were no clinical or roentgenologic signs of pyloric stenosis. The child was slightly anemic (hemoglobin value 54 per cent and 3,650,000 red blood cells) with abundant basophilic granulated erythrocytes. Roentgenologic examination of the skeleton revealed lead bands. The spinal fluid withdrawn after a fit of convulsions showed pleocytosis (17 cells per cubic millimeter with 94 per cent mononuclear cells). Lead was demonstrated in the blood and urine shortly after the patient's admission and a fortnight later. The vomiting decreased and ceased altogether after four weeks. The mother had used a lead cap for the protection of her nipples and an ointment containing lead for her breast.

WALLGREN, Stockholm, Sweden.

Correspondence

MUMPS: USE OF CONVALESCENT SERUM IN THE TREATMENT AND PROPHYLAXIS OF ORCHITIS

To the Editor:—I have just read the article on mumps by Dr. Alwin C. Rambar which appeared in the January 1946 issue of the AMERICAN JOURNAL OF DISEASES OF CHILDREN. I should like to inform you of my own observations concerning the treatment of that disease and of its terrible complication, orchitis.

From the inception of the disease I treat adults and adolescents with a sulfonamide drug, sulfapyridine (2-[paraaminobenzenesulfonamido]-pyridine, Soludagenan 693, prepared by the firm Specia Rhône Poulenc, Paris). I inject 1 Gm. of the drug intramuscularly both morning and evening. All the usual complications, such as orchitis, ovaritis, meningoencephalitis and rheumatism, have completely disappeared from my practice.

However, when I have to treat a patient suffering from orchitis I give an intramuscular injection of 1 Gm. of Soludagenan three times a day, and in serious cases I give an intravenous injection morning and evening of 0.5 to 1 Gm. of Soludagenan in 20 cc. of isotonic solution of sodium chloride.

I think that these results will be of interest in view of the frequency of this complication (24 per cent in France).

A. PAYCHÈRE, M.D., Paris, France.

15 Avenue de la Motte Picquet VII.

To the Editor:—Doctor Paychère's results in reducing the incidence of orchitis in adolescents and adults to zero are most interesting, although they are different from my own and from those of Haerem and others.

I have used sulfonamide compounds in the treatment of mumps orchitis, although the records of these patients are not now available. My recollection, however, is definitely that no noticeable benefit resulted. I doubt that the use of sulfonamide drugs parenterally would have produced results any different from those obtained by oral administration.

There are several reports in the literature of the use of the sulfonamide compounds in the treatment and prevention of orchitis. Haerem, in the *Military Surgeon* **92**:306-312, March 1943, treated 500 patients with mumps, dividing his groups so that 100 were controls, 100 each were treated with sulfathiazole, sulfapyridine and sulfanilamide, and 100 were given convalescent serum. His conclusions were that the use of the sulfonamide compounds in the treatment of mumps did not significantly diminish the length of the illness or the number of days of fever, and that it did not decrease the percentage of orchitis as compared with the controls and those who received serum therapy.

Twelve of my patients with orchitis were given penicillin, 20,000 units intramuscularly every three hours, with no beneficial effect.

ALWIN C. RAMBAR, M.D., Chicago.

1525 East Fifty-Third Street (15).

NEWS AND COMMENT

Appointments.—Dr. Kenneth S. Landauer, formerly a pediatrician of Geneva, N. Y., has been appointed Director of the Division of Medical Care for the National Foundation for Infantile Paralysis.

Directory of Pediatric Societies *

INTERNATIONAL

International Association of Preventive Pediatrics

President: Prof. S. Monrad, Dronning Louises Børnehospital, Copenhagen, Denmark.
Secretary: Dr. Daniel Oltramare, 15 Rue Lévrier, Geneva, Switzerland.

International Congress of Pediatrics

President: Dr. Henry F. Helmholz, Mayo Clinic, Rochester, Minn.
Secretary-General: Dr. L. Emmett Holt Jr., 477 First Ave., New York 16.
Canadian Committee:
Chairman: Dr. Alan Brown, Hospital for Sick Children, 67 College St., Toronto 2.
Secretary: Dr. S. G. Ross, 1390 Sherbrooke St. W., Montreal.
Place: New York. Time: Sept. 16-19, 1947.

International Congress for the Protection of Infancy

Secretary: Prof. G. B. Allaria, Corso Bramante 29, Torino 120, Italy.

Save the Children International Union

President: Mrs. Gordon Morier.
Secretary: Dr. Georges Thélin, 43 Quai Wilson, Geneva, Switzerland.

FOREIGN

Argentine Pediatric Society of Buenos Aires

President: Dr. Martin Ramón Arana, 1809 Rodriguez Peña, Buenos Aires.
General Secretary: Dr. Alfredo Larguia, Cerrito 1179, Buenos Aires.

Associação Paulista de Medicina, Secção de Pediatrias

President: Dr. Vicente Lara.
First Secretary: Dr. Armando de Arruda Sampaio.
Second Secretary: Dr. Luiz Augusto Monteiro Toledo, Av. Brigadeiro Luiz Antonio 393, 1° Andar, São Paulo, Brazil.
Time: Twelfth of every month, 8:30 p. m.

British Paediatric Association

President: Prof. G. B. Fleming, 13 Lynedoch Crescent, Glasgow.
Joint Secretary: Prof. Alan Moncrieff and Dr. Donald Paterson, Hospital for Sick Children, Great Ormond St., London, W. 1.

Danish Pediatric Society

President: Dr. E. Lenstrup, Copenhagen.
Secretary: Dr. Gjørup, Dronning Louises Børnehospital, Copenhagen.

Nederlandische Vereeniging voor Kindergeneeskunde

President: Dr. J. H. G. Carstens, Servaas Bolwerk 14, Utrecht.
Secretary: Dr. R. P. van de Kasteele, Lyccumplein 10, den Haag.
Place: Children's Hospital or Pediatric Clinic. Time: Three times a year.

* Secretaries of societies are requested to furnish the information necessary to make this list complete and to keep it up to date.

PALESTINE JEWISH MEDICAL ASSOCIATION, SECTION OF PHYSICIANS OF CHILDREN'S DISEASES

President: Prof. L. F. Meyer, 29 Toelsohn St., Tel Aviv.
Secretary: Dr. A Brünn, 9 Maazestre, Tel Aviv.

ROYAL SOCIETY OF MEDICINE, SECTION FOR THE STUDY OF DISEASE IN CHILDREN

President: Prof. Norman Capon, 49A Rodney St., Liverpool, England.
Secretary: Dr. J. N. O'Reilly, 46 Harley St., London, W. 1, England.
Place: 1 Wimpole St., London. Time: Fourth Friday of each month, 4:15 p. m.

SOCIEDAD CUBANA DE PEDIATRIA

President: Dr. Teodosio Valledor, Habana.
Secretary: Dr. Carlos Hernandez Miyares, Hospital Nuestra Señora de las Mercedes L y 21, Apartado, 2430, Habana.
Place: Cátedra de Clinica Infantil, Hospital Nuestra Señora de las Mercedas y Hospital Municipal de Infancia, Habana. Time: Last Wednesday of every month.

SOCIEDAD ECUADORIANA DE PEDIATRIA

President: Dr. Francisco de Icaza Bustamente.
Secretary: Dr. M. I. Gómez Lince, P. O. Box 693, Guayaquil.

SOCIEDAD MEXICANA DE PEDIATRIA

President: Dr. Luis Berlanga Berumen, Bucareli No. 85, Altos, Mexico.
Secretary: Dr. Jésus Alvarez de los Cobos, Ignacio Mariscal 124, Mexico.

SOCIEDAD DE PEDIATRIA DE CÓRDOBA

President: Dr. Juan Francisco Herrera, Córdoba, Argentina.
Secretary: Dr. Bernardo Serebrinsky, Dean Funes 2000, Esq. Ocaña (N.), Córdoba. Argentina.
Place: Comite pro Defenso del Niño, Dean Funes 2000, Córdoba, Argentina. Time: Once a month.

SOCIEDAD DE PEDIATRIA DEL LITORAL

President: Dr. Jose E. Celoria, Hospital Centenario, Rosario, Argentina.
Secretary: Dr. Gloria Lovell, Hospital Centenario, Rosario, Argentina.

SOCIEDAD DE PEDIATRÍA DE SANTIAGO DE CUBA

President: Dr. Antonio Béguez César, Sagarra 107, Santiago de Cuba.
Secretary: Dra. Susana Texdó Vaillant, Padre Pico 57, Santiago de Cuba.
Place: Colegio Médico. Time: Last Tuesday of every month.

SOCIEDAD VENEZOLANA DE PUERICULTURA Y PEDIATRIA

President: Dr. Pedro J. Alvarez.
Secretary: Dr. Ernesto R. Figueroa, 3a Avenida 10, Bella Vista, Caracas.
Place: Hospital Municipal de Niños Jose Manuel de los Rios, Caracas.

SOCIÉTÉ DE PÉDIATRIE DE PARIS

President: Dr. Leveuf, Paris, France.
Secretary: Dr. Jean Hallé, 10 bis Rue Pré aux Clercs, Paris, France.
Place: Hôpital des Enfants Maladies, 149 Rue de Sèvres. Time: 4:30 p. m., third Thursday of every month.

SWEDISH MEDICAL SOCIETY, SECTION FOR PEDIATRICS AND SCHOOL HYGIENE

President: Prof. Arvid Wallgren, 53 Strandvägen, Stockholm.
Secretary: Dr. Henning Magnusson, 58 Odengatan, Stockholm.
Place: Various clinics and hospitals in Stockholm and Uppsala. Time: Second Friday of each month (except summer).

URUGUAYAN SOCIETY OF PEDIATRICS

President: Dr. Jose Bonaba, Montevideo.
Secretary: Dr. Héctor Fossatti, Durazno 1882, Montevideo.
Place: Club Medico del Uruguay, Avenida Agraciado 1464 (Piso 13), Montevideo

NATIONAL

AMERICAN MEDICAL ASSOCIATION, SCIENTIFIC ASSEMBLY, SECTION ON PEDIATRICS

Chairman: Dr. John Aikman, 184 Alexander St., Rochester, N. Y.
Secretary: Dr. Gilbert J. Levy, 188 S. Bellevue Blvd., Memphis, Tenn.

AMERICAN ACADEMY OF PEDIATRICS

President: Dr. Jay I. Durand, 515 Cobb Bldg., Seattle, Wash.
Secretary: Dr. Clifford G. Grulee, 636 Church St., Evanston, Ill.
Place: Hotel William Penn, Pittsburgh. Time: Nov. 13-16, 1946.

AMERICAN HOSPITAL ASSOCIATION, MASSACHUSETTS HOSPITAL ASSOCIATION

Chairman: Dr. Frank Wing, Boston.
Secretary: Dr. W. Franklin Wood, McLean Hospital, Waverly 79, Mass.

AMERICAN PEDIATRIC SOCIETY

President: Dr. Harold K. Faber, 2361 Clay St., San Francisco.
Secretary-Treasurer: Dr. Henry G. Poncher, 1819 W. Polk St., Chicago 12.

CANADIAN SOCIETY FOR THE STUDY OF DISEASES OF CHILDREN

President: Dr. H. S. Little, 300 Dufferin Ave., London, Ontario.
Secretary-Treasurer: Dr. Elizabeth Chant Robertson, 67 College St., Toronto 2.

SOCIETY FOR PEDIATRIC RESEARCH

President: Dr. Mitchell I. Rubin, 219 Bryant St., Buffalo 9, N. Y.
Secretary: Dr. Robert F. Ward, Bellevue Hospital, New York 16.

SECTIONAL

INTERMOUNTAIN PEDIATRIC SOCIETY

President: Dr. Wesley H. Anderson, 2404 Washington Blvd., Ogden, Utah.
Secretary-Treasurer: Dr. F. M. Kriete, State Capitol, Salt Lake City.
Place: Salt Lake City General Hospital. Time: First Thursday of each month, 8 p. m.

NEW ENGLAND PEDIATRIC SOCIETY

President: Dr. James Marvin Baty, 1101 Beacon St., Brookline, Mass.
Secretary-Treasurer: Dr. Charles D. May, 300 Longwood Ave., Boston.
Place: Boston Medical Library. Time: Three meetings a year, occurring from September to May.

NORTH PACIFIC PEDIATRIC SOCIETY

President: Dr. Percy Guy, 502-2d Ave., Seattle, Wash.
Secretary: Dr. Aldis B. Johnson, 515 Cobb Bldg., Seattle, Wash.

NORTHWESTERN PEDIATRIC SOCIETY

President: Dr. George Kimmel, Redwing, Minn.
Secretary-Treasurer: Dr. Northrop Beach, 1009 Nicollet Ave., Minneapolis.
Place: Minneapolis, St. Paul, Duluth and Rochester. Time: January, April, July and October.

ROCKY MOUNTAIN PEDIATRIC SOCIETY

President: Dr. G. R. Fisher, 23 E. Pikes Peak Ave., Colorado Springs, Colo.
Secretary: Dr. Joseph H. Lyday, 1850 Gilpin St., Denver 2.

SOUTHERN MEDICAL ASSOCIATION, SECTION OF PEDIATRICS

Chairman: Dr. Stewart H. Welch, 117 S. 20th St., Birmingham 5, Ala.
Secretary: Dr. W. Ambrose McGee, 1601 Monument Ave., Richmond 20, Va.

STATE

ALABAMA PEDIATRIC SOCIETY

President: Dr. Jerome C. Chapman, 2160 Highland Ave., Birmingham.
Secretary-Treasurer: Dr. Ruth Berrey, 2021–6th Ave. N., Birmingham.

ARIZONA PEDIATRIC SOCIETY

President: Dr. W. P. Sherrill, 342 W. McDowell Rd., Phoenix.
Secretary: Dr. W. F. Schoffman, 926 E. McDowell Rd., Phoenix.
Place: Phoenix or Tucson. Time: At time of state meeting.

ARKANSAS STATE PEDIATRIC ASSOCIATION

Chairman: Dr. C. B. Billingsley, 1425 N. 11th St., Fort Smith.
Secretary: Dr. R. E. Weddington, 1425 N. 11th St., Fort Smith.

CALIFORNIA STATE MEDICAL SOCIETY, SECTION ON PEDIATRICS

Chairman: Dr. Charles W. Leach, 2000 Van Ness Ave., San Francisco 9.
Secretary: Dr. Chester I. Mead, 1930 Truxton Ave., Bakersfield.

FLORIDA STATE PEDIATRIC SOCIETY

President: Dr. Councill Rudolph, 103–5th St. S., St. Petersburg.
Secretary: Dr. Robert Blessing, 409 Blount Bldg., Ft. Lauderdale.
Place: Concurrent with state association convention and fall meeting.

GEORGIA PEDIATRIC SOCIETY

President: Dr. Alton Johnson, 102 E. Central Ave., Valdosta.
Secretary-Treasurer: Dr. Don F. Cathcart, 478 Peachtree St. N. E., Atlanta.
Place: Atlanta. Time: At time of annual state meeting.

HEZEKIAH BEARDSLEY PEDIATRIC CLUB OF CONNECTICUT

President: Dr. David Gaberman, 1179 Allyn St., Hartford, Conn.
Secretary: Dr. Herman Yannet, Southbury Training School, Southbury.

ILLINOIS STATE MEDICAL SOCIETY, SECTION ON PEDIATRICS

Chairman: Dr. Craig D. Butler, 715 Lake St., Oak Park.
Secretary: Dr. A. J. Fletcher, 139 N. Vermilion, Danville.

INDIANA STATE PEDIATRIC SOCIETY

President: Dr. K. T. Knode, 1105 E. Jefferson Bldg., South Bend.
Secretary-Treasurer: Dr. Matthew Winters, 621 Hume Mansur Bldg., Indianapolis.
Time: Two meetings a year.

IOWA PEDIATRIC SOCIETY

President: Dr. Arnold M. Smythe, 406–6th Ave., Des Moines.
Secretary-Treasurer: Dr. James Dunn, 414 Blackhawk Hotel, Davenport.

Louisiana State Pediatric Society

President: Dr. S. George Wolfe, 1560 Line Ave., Shreveport.
Secretary-Treasurer: Dr. W. C. Rivenbark, 1448 Louisiana Ave., New Orleans 15.

Medical Society of State of New York, Section on Pediatrics

Chairman: Dr. Carl H. Laws, 12 Pierrepont St., Brooklyn, N. Y.
Secretary: Dr. George R. Murphy, 292 Madison Ave., New York.

Medical Society of the State of Pennsylvania, Pediatric Section

Chairman: Dr. Elwood W. Stitzel, 403 Central Trust Bldg., Altoona, Pa.
Secretary: Dr. P. F. Lucchesi, Philadelphia Hospital, Philadelphia.

Michigan State Medical Society, Pediatric Section

Chairman: Dr. Donald J. Barnes, 3001 W. Grand Blvd., Detroit, Mich.
Secretary: Dr. Mark F. Osterlin, Central Michigan Children's Clinic, Traverse City.

Mississippi State Pediatric Society

President: Dr. Harvey F. Garrison Jr., 315 E. Capitol Pl., Jackson.
Secretary: Dr. Guy Verner, 126 N. Congress St., Jackson.

Nebraska Pediatric Society

President: Dr. John M. Thomas, 1418 Medical Arts Bldg., Omaha 2.
Secretary-Treasurer: Dr. Gerald C. O'Neil, 640 City National Bank Bldg., Omaha.
Place: As announced by committee. Time: Third Thursday of each month from October to June, inclusive. Dinner at 6 p. m.

New Mexico State Pediatric Society

President: Dr. M. K. Wylder, 221 W. Central Ave., Albuquerque.
Secretary-Treasurer: Dr. Ly Werner, 221 W. Central Ave., Albuquerque.

North Carolina Pediatric Society

President: Dr. Charles R. Bugg, Professional Bldg., Raleigh.
Secretary: Dr. Charles F. Williams, 817 Hillsboro St., Raleigh.

Northern California Pediatric Society

President: Dr. Edith M. Meyers, 431–30th St., Oakland.
Secretary: Dr. A. L. Gleason, 411–29th St., Oakland 9.
Place: San Francisco. Time: Second Thursday of February, April, September and November.

Oklahoma State Pediatric Society

President: Dr. G. R. Russell, 604 S. Cincinnati Ave., Tulsa.
Secretary: Dr. Luverne Hays, 108 W. 6th St., Tulsa.
Place: With Oklahoma State Medical Association. Time: Annual Meeting.

South Carolina Pediatric Society

President: Dr. George D. Johnson, Spartanburg.
Secretary-Treasurer: Dr. B. O. Ravenel, Roper Hospital, Charleston.

Tennessee Pediatric Society

President: Dr. F. T. Mitchell, 376 S. Bellview, Memphis.
Secretary-Treasurer: Dr. W. O. Vaughan, 2103 Hayes St., Nashville 5.
Time: Second Monday in April.

Texas Pediatric Society

President: Dr. Max Woodward, 202 N. Travis St., Sherman.
Secretary-Treasurer: Dr. John E. Ashby, 3610 Fairmount Ave., Dallas 4.

Virginia Pediatric Society

President: Dr. Emily Gardner, 1100 W. Franklin St., Richmond 20.
Secretary: Dr. Louise Galvin, 214 S. Boulevard, Richmond 21.

West Virginia State Medical Society, Section on Pediatrics

President: Dr. Jack Basman, 1021 Quarrier St., Charleston.
Secretary: Dr. Harry E. Baldock, Medical Arts Bldg., Charleston.

LOCAL

Academy of Medicine of Cleveland, Pediatric Section

Chairman: Dr. J. I. Hartman, 10515 Carnegie Ave., Cleveland.
Secretary: Dr. Alexander N. Freed, 2012 W. 25th St., Cleveland.
Place: Cleveland Medical Library Bldg. Time: 8:15 p. m., October, December, February and April.

Academy of Medicine, Toronto, Section of Pediatrics

President: Dr. J. H. Ebbs, 13 Queen's Park, Toronto, Canada.
Secretary: Dr. J. F. McCreary, 170 St. George St., Toronto, Canada.
Place: Academy of Medicine. Time: 8:30 p. m., third Thursday of each month.

Baltimore City Medical Society, Pediatric Section

Chairman: Dr. Charles O'Donovan Jr., 5 E. Read St., Baltimore.
Secretary: Dr. T. Campbell Goodwin, 16 E. Biddle St., Baltimore.

Bronx Pediatric Society

President: Dr. Walter Levy, 12 E. 88th St., New York.
Secretary: Dr. Joseph Blasenstein, 960 Grand Concourse, New York.
Place: Concourse Plaza Hotel, 161st St. and Grand Concourse. Time: Second Wednesday of each month, except June, July, August and September.

Brooklyn Academy of Pediatrics

President: Dr. Lambert Krahulik, 14 Sidney Pl., Brooklyn.
Secretary: Dr. Joseph Battaglia, 713 Bushwick Ave., Brooklyn 21.
Place: Granada Hotel. Time: 8:45 p. m., fourth Wednesday of February, March, April, May and November.

Buffalo Pediatric Society

President: Dr. Douglas P. Arnold, 159 Bidwell Parkway, Buffalo, N. Y.
Secretary: Dr. Richard A. Downey, 786 Forest Ave., Buffalo 9, N. Y.
Place: Children's Hospital, 219 Bryant St. Time: 8:30 p. m., first Monday of each month from September to June.

Central New York Pediatric Club

President: Dr. Arthur W. Benson, 2 St. Paul St., Troy.
Secretary: Dr. Frank J. Williams, 58 S. Swan St., Albany.
Places: Various cities in New York. Time: Third Tuesday of April and October.

Chicago Pediatric Society

President: Dr. Joseph Greengard, 4753 Broadway, Chicago 40.
Secretary: Dr. Alvah L. Newcomb, 723 Elm St., Winnetka, Ill.
Place: Children's Memorial Hospital, 710 Fullerton Ave. Time: Third Tuesday of each month, October to May inclusive.

Cincinnati Pediatric Society

President: Dr. Leo S. Friedman, 666 Rockdale Ave., Cincinnati 29.
Secretary: Dr. George Renner, 3144 Jefferson Ave., Cincinnati.
Place: Children's Hospital, Elland Ave., Cincinnati. Time: On call.

Dallas Pediatric Society

President: Dr. O. René Caillet, 4325 Cole Ave., Dallas, Texas.
Secretary-Treasurer: Dorothy Wyvell, Bradford Memorial Hospital for Babies, Texas.
Place: Children's Medical Center. Time: 1 p. m., third Saturday and 8:30 p. m., the first Thursday of each month.

Detroit Pediatric Society

President: Dr. Otto Grob, 651 Fisher Bldg., Detroit 2, Mich.
Secretary: Dr. Harold B. Rothbart, 773 Fisher Bldg., Detroit 2, Mich.
Place: Variable. Time: Third Wednesday of each month.

Houston Pediatric Society

President: Dr. Raymond Cohen, 2300 Caroline St., Houston, Texas.
Secretary: Dr. Betty Moody, 526 Richmond Rd., Houston, Texas.
Place: River Oaks Country Club. Time: 7:30 p. m., fourth Monday of each month.

Kansas City (Missouri) Pediatric Society

President: Dr. Harry M. Gilkey, 1624 Professional Bldg., Kansas City.
Secretary: Dr. Leland Speer, 1022 Parkway, Kansas City.
Place: Kansas City General Hospital. Time: On call.

Los Angeles County Medical Association, Pediatric Section

President: Dr. Albert L. Hill, 1401 S. Hope St., Los Angeles.
Secretary-Treasurer: Dr. Robert Simonds, 1925 Wilshire Blvd., Los Angeles.
Place: Los Angeles County Medical Headquarters, 1925 Wilshire Blvd. Time: Second Monday of February, April, June, October and December.

Medical Society of the County of Kings and the Academy of Medicine of Brooklyn, Pediatric Section

President: Dr. Henry Rascoff, 895 Eastern Parkway, Brooklyn.
Secretary: Dr. Harold Levy, 750 St. Marks Ave., Brooklyn.
Place: 1313 Bedford Ave., Brooklyn. Time: 9:00 p. m., fourth Monday of each month.

Medical Society of the County of Queens, Inc., Section on Pediatrics

Chairman: Dr. Meyeron Coe, 217-02-91st Ave., Queens Village, N. Y.
Secretary-Treasurer: Dr. Louis Appel, 143-42 Cherry Ave., Flushing, N. Y.
Place: Queens County Medical Bldg., Forest Hills, N. Y. Time: Third Monday of October, January, March and May.

Medical Society of the District of Columbia, Section on Pediatrics

President: Dr. John Washington, 2203 Wyoming Ave., Washington, D. C.
Secretary-Treasurer: Dr. George Maksim, 1418 Good Hope Rd. S.E., Washington, D. C.
Place: Medical Society Bldg., 1718 M St. N. W. Time: 8 p. m., third Thursday of October, January, March and May.

Memphis Pediatric Society

President: Dr. Kinsey M. Buck, 1193 Madison Ave., Memphis, Tenn.
Secretary-Treasurer: Dr. Barton Etter, 1024 Madison Ave., Memphis, Tenn.
Place: Memphis Country Club. Time: 8 p. m., Dec. 13, 1946.

Milwaukee Pediatric Society

President: Dr. G. H. Fellman, 231 W. Wisconsin Ave., Milwaukee.
Secretary-Treasurer: Dr. R. P. Showalter, 411 E. Mason St., Milwaukee 2.
Place: Milwaukee Children's Hospital. Time: Second Wednesday in February, April, June, October and December.

New York Academy of Medicine, Section of Pediatrics

Chairman: Dr. Robert O. Du Bois, 122 E. 76th St., New York.
Secretary: Dr. Harold W. Dargeon, 1095 Park Ave., New York.
Place: New York Academy of Medicine, 2 E. 103d St. Time: Second Thursday of each month from November to May, inclusive, 8:30 p. m.

Oklahoma City Pediatric Society

President: Dr. William M. Taylor, 625½ N. W. 10th St., Oklahoma City.
Secretary: Dr. Jeanne McKinnon-Shofstall, 1019 N. Lee St., Oklahoma City.
Place: Oklahoma Club. Time: Third Thursday of each month.

Philadelphia Pediatric Society

President: Dr. Waldo E. Nelson, Temple University School of Medicine, Philadelphia.
Secretary: Dr. Sherman Little, 1740 Bainbridge St., Philadelphia 46.
Place: College of Physicians, 19 S. 22d St. Time: 8:30 p. m., second Tuesday in October, December, February and April.

Pittsburgh Pediatric Society

President: Dr. Elwood Stitzel, 403 Central Trust Bldg., Altoona, Pa.
Secretary-Treasurer: Dr. C. J. Stoecklein, Medical Arts Bldg., Pittsburgh 13.
Place: Pittsburgh Academy of Medicine. Time: Second Friday in October, December, February and April.

Richmond Pediatric Society

President: Dr. Edwin L. Kendig Jr., 828 W. Franklin St., Richmond 20, Va.
Secretary-Treasurer: Dr. Thomas S. Chalkley, 1200 E. Broad St., Richmond, Va.
Place: Medical College Hospital. Time: 8 p. m., third Thursday of each month, except June, July and August.

Rochester Pediatric Society

President: Dr. William L. Bradford, 260 Crittenden Blvd., Rochester 7, N. Y.
Secretary-Treasurer: Dr. Donald D. Posson, 222 Chili Ave., Rochester 11, N. Y.
Place: Rochester Academy of Medicine or arrangement by program committee.
Time: Third Friday of each month from October to May.

St. Louis Pediatric Society

President: Dr. Joseph C. Jaudon, 337 N. Euclid Ave., St. Louis.
Secretary-Treasurer: Dr. Gilbert B. Forbes, 500 S. Kingshighway, St. Louis 10.
Time: Second Thursday of each month from October to May, inclusive.

Seattle Pediatric Society

President: Dr. Norman W. Murphy, 1300 Madison St., Seattle 4.
Secretary: Dr. David M. Harris, 630 Medical Arts Bldg., Seattle 1.
Place: College Club. Time: Third Friday of each month from September to June at 6:30 p. m.

Southwestern Pediatric Society

President: Dr. Robert J. Dostal, 710 Wilshire Blvd., Santa Monica, Calif.
Secretary: Dr. H. M. Van Dyke, 541 E. Broadway, Long Beach, Calif.
Place: University Club of Los Angeles. Time: 6:30 p. m., first Wednesday in January, March, May, September and November.

University of Michigan Pediatric and Infectious Disease Society

President: Dr. Park Bradshaw, Muskegon, Mich.
Secretary: Dr. Harry A. Towsley, 1313 E. Ann St., Ann Arbor, Mich.
Place: University Hospital, Ann Arbor, Mich. Time: Oct. 25-26, 1946.

Westchester County Medical Society, Pediatrics Section (New York)

President: Dr. John B. Ahouse, 27 Ludlow St., Yonkers, N. Y.
Secretary-Treasurer: Dr. Elvira Ostlund, 64 Highland Rd., Rye, N. Y.
Place: Hospitals of Westchester County. Time: Third Thursday in November, January, March and May.

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